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ABSTRACT

Abstracts of 130 research projects in alcohol and drug programs in California are presented in this document. The projects described in this directory show the extent and diversity of current alcohol and drug research within the state. Each abstract lists the principal investigator with his or her title, institution, and address; co-principal investigators (if any); research project name; project dates; financial supporters; and a description of the project. The abstracts show that the funds supporting the research come from a wide range of federal, state, charitable, and private organizations. The directory is arranged alphabetically by principal investigators within separate sections on alcohol, alcohol and drug, and drug research. Also included are indices by subject and author. Although basic research projects on Acquired Immune Deficiency Syndrome are not included in the directory, sources for this information are provided. (ABL)

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ALCOHOL AND DRUG RESEARCH IN CALIFORNIA 1987

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ALCOHOL AND DRUG RESEARCH IN CALIFORNIA — 1987

This Directory was compiled and edited by
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ADP 87-2

March 1987

PREFACE

We wish to thank the 161 principal and co-principal investigators who contributed the 130 abstracts to the Department of Alcohol and Drug Programs second directory of alcohol and drug research in California. The projects described in this directory show the extent and diversity of current alcohol and drug research within the state. The funds supporting the research come from a wide range of federal, state, charitable and private foundations.

The directory is arranged alphabetically by Principal Investigators within separate sections on alcohol and drug research. Also included are indices by subject and author which may be useful in locating specific investigators and activities.

TABLE OF CONTENTS

	Page
ALCOHOL	1
ALKANA, RONALD L., Pharm.D., Ph.D.	
#1 Low Level Hyperbaric Ethanol Antagonism	1
#2 Temperature Dependence of Ethanol Depression	2
AMES, GENEVIEVE, M., Ph.D.	
#1 An Exploration of a Family-level Model for Prevention of Alcohol Problems	3
#2 Alcohol and Mexican-American Families	4
#3 Indicators of Women's Alcoholism and Alcohol Related Problems	5
BARCHAS, JACK D., M.D.	
Neuroregulators and Alcohol Abuse	6
BIKLE, DANIEL, M.D., Ph.D.	
Bone Disease of Alcoholics	7
BLOOM, FLOYD E., M.D.	
#1 Event-related Brain Potentials and the Inheritability of Alcoholism	8
#2 CNS Effects of Alcohol: Cellular Neurobiology	9
BROWN, SANDRA A., Ph.D.	
#1 Adolescent Alcohol Treatment Outcome: Recovery Patterns	10
#2 Expectancies in Primary and Secondary Alcohol Abuse	11
CAETANO, RAUL, M.D., Ph.D.	
Black and Hispanic Drinking Patterns	12
EHLERS, CINDY L., Ph.D.	
Development of a Rat Event-Related Potential Model for the Study of Acute and Chronic Effects of Ethanol	13
EPSTEIN, LEONARD, MSW	
California First DUI Offender Evaluation Project	14
FOOTE, STEPHAN J., Ph.D.	
Systematic Neuropharmacology	15

Page

GILBERT, M. JEAN, Ph.D.
#1 Alcohol Expectancies Among Mexican-American Female Alcoholics 16
#2 Alcohol Expectancies, Alcohol Abuse, and Alcohol Dependency Among Mexican and Mexican-American Treatment Clients 17
#3 Scholar in Hispanic Alcohol Studies 18

GORDON, ADRIENNE S., Ph.D.
#1 Chronic Effects of Ethanol on Neural Cells in Culture . . . 19
#2 Ethanol Tolerance and Dependence at a Cellular Level 20

GORELICK, DAVID A., M.D., Ph.D.
Role of Alcohol Withdrawal in Alcoholism Outcome 21

GREENBERG, DAVID A., M.D., Ph.D.
Interactions of Ethanol and Related Drugs with Ion Channels and Neurotransmitter Receptors 22

HALSTEAD, CHARLES S., M.D.
Folate Metabolism in the Alcoholic Pig 23

HANSEN, WILLIAM B., Ph.D.
Adolescent Alcohol Prevention Trial (AAPT) 24

HELANDER, CLIFFORD J., A.B., M.P.A.
Post-disqualification Control of DUI Offenders 25

HILTON, MICHAEL E., Ph.D.
#1 Contra Costa County General Population Survey 26
#2 The Epidemiology of Drinking Problems: Analysis of the 1984 National Alcohol Survey 26

HOLDER, HAROLD D., Ph.D.
Environmental Approaches to Prevention 27

KLATSKY, ARTHUR L., M.D.
Alcohol Consumption and Multiphasic Health Examination Findings 28

KOOB, GEORGE F., Ph.D.
Behavioral Pharmacology 29

LOWE, LOIS, Ph.D.
Reanalysis of the San Francisco Black Drinking Practices Study Data 30

McGIVERN, ROBERT F., Ph.D.
Prenatal Alcohol: Endocrine and Sexually Dimorphic Effects 31

Page

MEDICINE, BEATRICE, Ph.D.
Sobriety Maintenance Among Sioux (Lakota) Indians: Gender Differences in Drinking Styles Among Natives (Plains Groups) 32

MILNER, DR. R. J.
The Effects of Ethanol on Brain Development 33

MOOS, RUDOLPH H., Ph.D.
#1 Evaluating Alcoholism-Inducing Community Settings 34
#2 Life Stressors and Problem Drinking Among Older Adults 35

MOSHER, JAMES F., J.D.
#1 Community Guide to Alcohol Availability Laws and Regulations 36
#2 Prevention Research: ABC Policies on Drunk Driving 36

MOSKOWITZ, JOEL, Ph.D.
Survey of High School Alcohol Policies 37

NASATIR, DAVID, Ph.D.
College Student Drinking Study 38

NEVILLE, HELEN J., Ph.D.
Human Evoked Responses 39

O'CONNOR, MARY J., Ph.D.
Development of Infants Whose Mothers Drink 40

PAIGEN, KENNETH, Ph.D.
Distant Regulatory Genes in Drosophila Studies of Mammalian Gene Regulation 41

PARKER, DOUGLAS A., Ph.D.
Alcohol Use and Physical Health 42

PFEFFERBAUM, ADOLPH, M.D.
CNS Deficits: Interaction of Age and Alcoholism 43

RATZ, MICHAEL, M.A.
Development of an Improved Management Control System for DUI Drivers 44

RIVIER, CATHERINE, Ph.D.
Neuroendrocrine Effects of Ethanol 45

ROIZEN, RON, M.A.
Mental Health Client Study: Part of the Community Laboratory Project 46

Page

ROOM, ROBIN, Ph.D.
Epidemiology of Alcohol Problems 47

SALTZ, ROBERT, Ph.D.
Server Intervention Project 48

SCHUCKIT, MARC A., M.D.
#1 Center for Clinical Research in Alcoholism 49
#2 Less Intense Reaction to Brain Depressants in Sons of Alcoholics 50
#3 EEG Markers of Alcohol Intoxication in High and Low Risk Subjects 51

SIGGINS, GEORGE ROBERT, Ph.D.
Neuronal and Synaptic Actions of Alcohol 52

STEPHENS, CHERYL, D.P.H.
#1 San Francisco General Hospital Emergency Room Study 53
#2 Contra Costa County Emergency Room Study 53
#3 Contra Costa County Hospital Emergency Room Casualty Study 54
#4 Alcohol Consumption, Injuries and Medical Problems: A Study of Emergency Room Studies 55
#5 Alcohol Consumption, Social Support, and Infant Outcomes 55

TASHIMA, HELEN, M.A., M.S.W.
DUI Offender Tracking System (DOTS) Study 56

TEMPLE, MARK T., Ph.D.
Alcohol Use and Aging: A 20 Year Follow-up Study 57

VALE, WYLIE W., Ph.D.
Neuroendrocrine Effects 58

VOURAKIS, CHRISTINE, D.N.Sc. Candidate
Some Aspects of Treatment of Women Alcoholics: All-Women Versus Mixed-Sex AA Meetings 59

WAGENAAR, ALEXANDER, Ph.D.
Alcohol Related Traffic Crashes 60

Page

WEISNER, CONNIE, D.P.H Candidate
Alcohol Problems and Pathways to Treatment 61

YESAVAGE, JEROME A., M.D.
Pilot Performance and Alcohol 62

YOSHIDA, AKIRA, Ph.D.
Human Alcohol Dehydrogenase and Aldehyde Dehydrogenase 64

ALCOHOL AND DRUG 65

BITONTI, CHRISTINE
Women in Transition Prevention Evaluation 65

ESTEP, RHODA, Ph.D.
Impaired Small Town Physicians and Their Spouses 66

IRWIN, CHARLES E., JR., M.D.
Risk Taking Behaviors in Adolescents 67

KING, LEWIS, Ph.D.
Developmental Issues in Alcohol and Drug Dependency 68

STALL, RONALD, Ph.D., M.P.H.
Alcohol and Drug Use Consumption Patterns and AIDS 69

DRUGS 70

ANGLIN, M. DOUGLAS, Ph.D.
#1 The Natural History of Narcotic Addiction: A 25-Year Follow Up 70
#2 Addict Career Histories: Processes and Patterns 71
#3 Optimization of Legal Supervision for Chronic Addict Offenders 72
#4 California Drug Abuse Information and Monitoring Project (DAIMP) 73

Page

BAUMRIND, DIANA, Ph.D.
Stress Reactivity: Familial Antecedents of Adolescent Adjustment 74

BERNAL, GUILLERMO, Ph.D.
Intergenerational Family Therapy with Drug Abusers 76

BROWN, JOHN K., Ph.D.
Community Drug Identification Service 78

CASTAGNOLI, NEAL, JR., Ph.D.
#1 Bioactivation of Tert-Allylamines (MPTP) to Neurotoxind 79
#2 Iminium Metabolities from Tertiary Amines (Phencyclidine) 79

CHO, ARTHUR K., Ph.D.
#1 Chemical Pharmacology of MDA and MDMA 80
#2 Chemistry of Phencylidine Metabolism 80

DEVINE, MARSHA L., M.A.
Cannabis Therapeutic Program 81

EL SHAMI, A. SAID,
#1 Serum Morphine RIA Kit 82
#2 Cocaine Metabolite RIA Kit for Drug Abuse 82

ELLICKSON, PHYLLIS L., Ph.D.
Project Alert: A Smoking and Drug Prevention Experiment 83

FIELDS, HOWARD, M.D., Ph.D.
Neuronal Substrate of Opiate Analgesia 84

FLAY, BRIAN R., D.Phil
#1 Television School and Family Project (TVSP) 85
#2 Television School and Family Project 86

FRAWLEY, P. JOSEPH., M.D.
Chemical Aversion Therapy in the Treatment of Cocaine Dependence as Part of an Overall Treatment Program 87

GEYER, MARK A., Ph.D.
Monoamines and Hallucinogen's Effects on Rat Behavior . . . 88

GOLDSTEIN, AVRAM, M.D.
Endogenous Opioids and Their Receptors 89

Page

JONES, REESE T., M.D.
#1 Marijuana Smoking Typography Aid Dose Regulation 90
#2 Effects of the Tolerance--Dependence on Marijuana Smoking 91
#3 Cocaine Pharmacokinetics and Pharmacodynamics 92
#4 Drug Dependence Clinical Research Program 93
#5 Neuropsychopharmacology of Altered Consciousness 94

KOOB, GEORGE F., Ph.D.
#1 Central Mechanisms of Opiate Reinforcement 95
#2 Neuronal Substrates of Cocaine Reward 96

LEE, NANCY M., Ph.D.
B-Endorphin Receptor: Relationship to Mu and Delta Bindings 97

LIDDLE, HOWARD A., Ed.D.
Structural-Strategic Family Therapy with Adolescent Drug Abusers 98

LOH, HORACE H., Ph.D.
Neurochemical Basis of Narcotic Addiction 99

MALONE, MARVIN H., Ph.D.
Pharmacologic Definition of the Opioid Receptor Selectivity of Selected Aminotetralin Analogs 100

McCLOSKEY, CHESTER M., Ph.D.
Preparation of Delta9THC and LAAM 101

MOORE, JOAN W., Ph.D.
Youth Subculture Versus Individual Factors in Adult Drug Use 102

MORGAN, DAVID G., Ph.D.
Neurotransmitter Receptors in Aging Mammalian Brain 103

NEWMEYER, JOHN A., Ph.D.
AIDS Risk Reduction for Needle-using Drug Users 104

RAPOPORT, HENRY, Ph.D.
Bioorganic Chemistry of the Opium Alkaloids In Vitro 105

REBERT, CHARLES S., Ph.D.
Neurotoxicity of Marijuana in Subhuman Primate 106

ROSENBAUM, MARSHA, Ph.D.
Methadone Treatment: A Study of County Policy Change . . . 107

SADAVA, DAVID, Ph.D.
Effects of Methadone Addiction on Rats 108

Page

SADEE, WOLFGANG, Ph.D.
Opioid Receptor Binding In Vivo and Effects in Rats and Neuroblastoma Cells in Culture 109

SEGAL, DAVID S., Ph.D.
#1 Behavioral Pharmacology of Opiate-like Neuropeptides 110
#2 Behavioral Pharmacology of Acute and Chronic Amphetamine 111

SIGGINS, GEORGE R., Ph.D.
Morphine-like Brain Peptides: Cellular Neurobiology 112

SORENSEN, JAMES L., Ph.D.
#1 From Methadone Maintenance to Abstinence 113
#2 Community Network Approach to Drug Abuse Treatment 114
#3 Substance Abuse Component of Substance Abuse and Mental Health in AIDS Center 115
#4 AIDS Prevention with Drug Abusers: A Psychoeducational Approach 116

STEVENS, KAREN S., M.A.
Identification of Opiate Reward Receptors 117

STRANTZ, IRMA H., Dr. P.H.
#1 Los Angeles County HTLV-III Seroprevalence Study 118
#2 Current Trends and Patterns of Drug Abuse in Los Angeles County, 1982-1985 119
#3 Client Outcome from Drug Treatment January 1984-December 1985 120
#4 Drug Abuse Treatment Client Satisfaction Survey 121

TASHKIN, DONALD P., M.D.
Pulmonary Effects of Habitual, Heavy Marijuana Use 122

TENNANT, FOREST S., Jr., M.D., DR. P.H.
#1 Retention Time of Anabolic Steriods in Urine 123
#2 Step-wise Withdrawal Treatment for Cocaine and Nicotine Dependence 123
#3 Laam Maintenance for Persons Who Fail Methadone Treatment . . 123
#4 Urine Testing of Adolescents by Parents 124
#5 Identification and Prevention of AIDS in Intravenous Drug Users 124

WALDORF, DANIEL, M.A.
Cocaine Cessation: Treated and Untreated 125

WATTERS, JOHN K., Ph.D.
#1 HIV Seroprevalence and Sequellae Among I.V. Users in Two Cities 126
#2 AIDS Risk Reduction for Needle-Using Drug Users 104

Page

WESSON, DONALD R., M.D.
Naltrexone Treatment of Opiate Dependence 127

YESAVAGE, JEROME A., M.D.
Pilot Performance and Tetrahydrocannabinol 128

RESEARCH ADVISORY PANEL 130

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS) 131

AUTHOR INDEX 132

SUBJECT INDEX 134

ALCOHOL

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RESEARCH PROJECT #1: LOW LEVEL HYPERBARIC ETHANOL ANTAGONISM
PROJECT DATES: 04/1/83 -- 03/31/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

Previous work in our laboratory suggest that low level hyperbaric environments ($\leq$12 atmospheres absolute) antagonize ethanol sleep-time in mice by directly offsetting its fluidizing action on biological membranes.

The specific aims of the present proposal are to:

1) Extend the investigation of hyperbaric antagonism to sub-hypnotic ethanol doses using locomotor activity, psychomotor performance (moving belt) and isolation induced aggression;

2) Establish whether hyperbaric environments can antagonize the well defined membrane-related inhibition of Na^+, Ka^+-ATPase activity and stimulation of ecto-5'-nucleotidase activity in isolated systems and determine if the action is membrane specific; and

3) Use hyperbarics as a "classical pharmacological antagonist"; begin to distinguish biochemical effects of ethanol that mediate, rather than accompany, the development of acute intoxication, tolerance, and physical dependence.

The latter will include tests of the correlations between the degree of antagonism on behavioral measures with the degree of antagonism on selected biochemical effects including Na^+, K^+ATPase activity, neurotransmitter metabolism (dopamine, norepinephrine and serotonin) and membrane lipid changes (cholesterol, fatty acids, phospholipids). To accomplish these aims, experiments will be conducted in environments of 1 atmosphere absolute (ATA) air, 1 ATA helium-oxygen and 12 ATA helium-oxygen using C57 Bl/6J, BALB c/J, DBA/1J, TO Swiss and Swiss Webster mice and *E.coli* cultures as subjects. *In vitro* preparations from C6 glioma and mouse brain homogenates will also be tested at pressures up to 18 ATA. Our long term goals are to increase understanding of the causes of alcohol abuse and alcoholism by identifying the membrane-related sequence of biochemical and physiological events responsible for mediating ethanol's behavioral effects.

RESEARCH PROJECT #2: TEMPERATURE DEPENDENCE OF ETHANOL DEPRESSION
PROJECT DATES: No dates given
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

A recent investigation in our laboratory indicated that changes in environmental, and more directly, rectal temperature altered the brain's sensitivity to an anesthetic dose of ethanol in male C57 mice. Subsequent experiments suggested that the temperature dependence also extends to subhypnotic and lethal ethanol doses. The goal of the proposed research is to extend these findings by examining the scope and importance of temperature in determining ethanol potency and brain sensitivity in mammals. Experiments will be conducted in C57 Bl/7j, DBA 2/BALBc/j and SWR/j mice and guinea pigs (Hartley). Animals will be injected with ethanol (or saline). Rectal temperature will be monitored during post-ethanol exposure to room temperature control ($22^{+\circ}$C) or one of several experimental temperature (-4 to 41°C) environments. The interactive effect of temperature on ethanol's behavioral and physiological effects will be monitored using traction behavior and tilt-plane performance, locomotor activity, sleep-time, mortality, respiratory rate and signs of tolerance. Blood and brain ethanol concentrations will be determined in selected experiments in order to measure brain sensitivity to ethanol at the different temperatures and the contribution of altered ethanol elimination and/or distribution in mediating the effects of temperature on ethanol intoxication.

These experiments will:

1) Determine the generality and extent of the temperature-dependence across strains, species, sexes and doses (subhypnotic, hypnotic, lethal);

2) Establish whether body temperature changes can reduce lethality from ethanol in combination with other depressant drugs;

3) Investigate the relationship between body temperature while intoxicated and genetically based sensitivity to ethanol;

4) Assess whether temperature can alter the rate of development or degree of ethanol tolerance.

This information will have important impact on our knowledge regarding ethanol's mechanism of action, ethanol's interactions with other drugs and the treatment of ethanol or ethanol-combination overdoses.

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RESEARCH PROJECT #1: **AN EXPLORATION OF A FAMILY-LEVEL MODEL FOR PREVENTION OF ALCOHOL PROBLEMS**

PROJECT DATES: 11/1/83 -- 11/1/87

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The primary goal of this project is to explore and identify family practices which either inhibit or contribute to the development and maintenance of alcohol-related problems. Viewing the family as a system, it is proposed that learned and adaptive responses to alcohol use can be examined and organized within the following categories:

1) Cultural patterning;

2) Strategies for basic family survival; and

3) Individual need fulfillment.

Using anthropological methods of naturalistic observation, open-ended interviews and life history assessment, each participating family will be studied in their home during six extended visits over a time span of four to six months.

Forty families will be selected from two populations considered at high risk for developing alcohol problems; blue collar unemployed and United States Navy. A preliminary drinking survey of a larger representative sample of these populations will also be taken. This study will provide the basis for family-level approaches to alcohol prevention to be developed in the fourth year of the study.

Co-principal Investigators

JUANA MORA, Ph.D.
KITTY CORBETT

RESEARCH PROJECT #2: **ALCOHOL AND MEXICAN-AMERICAN FAMILIES**
PROJECT DATES: 04/1/86 -- 03/31/89
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

This is a study of drinking practices and alcohol-related problems within Mexican-American families. It builds on prior findings that Mexican-American men have high rates of alcohol use, with consequent alcohol-related problems for their families. The study takes into account the special circumstances, characteristics, and cultural premises of this population. Specifically, we address the relationships among drinking behavior, family systems, and the sociocultural context in which they are situated. Using the Principal Investigator's family-level cultural approach in conjunction with social network analysis, the study will:

1) Develop knowledge about family level processes that inhibit or support the development and maintenance of drinking and alcohol-related problems in Mexican American families;

2) Develop knowledge about individual and family social networks and their relationship to drinking practices and related problems in Mexican American families;

3) Relate the cultural and organizational drinking ecology of the community where the study population lives to their drinking practices and related problems; and

4) Develop both a strategy for dissemination of information and family-oriented, culturally appropriate prevention guidelines based on the study's findings.

The research design calls for a three-year study using multiple methods and research stages. The first stage is a community ethnography. The second stage involves a survey of husbands and wives from 200 families in the community. The third stage will consist of case studies of 20 families selected from those surveyed, where fathers are moderate or heavier drinkers. The final stage and ultimate goal is to develop a set of programmatic guidelines for the prevention of alcohol-related problems in the Mexican-American population.

Co-principal Investigators

LENNEA KLEE, Ph.D.
ROBERT SALTZ, Ph.D.

RESEARCH PROJECT #3: **INDICATORS OF WOMEN'S ALCOHOLISM AND ALCOHOL RELATED PROBLEMS**

PROJECT DATES: 10/1/86 -- 04/1/88

FINANCIAL SUPPORT: California Department of Alcohol and Drug Programs, Health and Welfare Agency

DESCRIPTION OF PROJECT:

The purpose of this study is to develop a severity/frequency scale that can be used to effectively determine indicators of alcoholism and alcohol problems across a range of women in the population, including women from various ethnic groups, age groups, socioeconomic statuses, sexual orientations, and geographic locations. Our research strategy has three components:

1) A review of the existing literature and interviews with key informants who are knowledgeable of women's alcohol related problems;

2) Systematic ethnographic interviews with representative women in treatment for alcohol related problems; and

3) A countywide survey of more than 1,000 women for the purpose of measuring the prevalence of alcohol consumption, alcohol problems, and the influence that social context has in both.

Thus, the three components of this project permit data collected in open-ended interviews with key informants who are providers, researchers, and advocates, to be presented to and evaluated by representative women actually in treatment, ultimately creating survey items that most effectively reflect women's real experiences.

Co-principal Investigator

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RESEARCH PROJECT: **NEUROREGULATORS AND ALCOHOL ABUSE**
PROJECT DATES: 07/01/84 -- 06/30/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The tryptolines are the class of compounds which arise from the chemical condensation reaction between indoleamines and aldehydes. Indoleamines are naturally-occurring neurotransmitters and neuromodulators (e.g., serotonin) which are found in the nervous system of all mammals including man. Aldehydes are frequently produced as transient biochemical intermediates in mammalian tissues, but they are often short-lived and rapidly metabolized. Interest in the physiological significance of these condensation products stems from three sources:

1. The ease with which the condensation reaction proceeds in vitro under physiological conditions has initiated speculation that the compounds could occur naturally in mammalian tissues. The neuropharmacological effects of tryptolines have added to this speculation by prompting the suggestion that the in vivo presence of such compounds could have important implications for the regulation of cerebral neurotransmission.

2. Interest in this class of compounds has also stemmed from reports on their ability to displace tritiated diazepam from the benzodiazepine receptor in brain membrane preparations. These reports have given rise to speculation that compounds of this class could be the unidentified endogenous ligand for the benzodiazepine receptor.

3. There has also been speculation that the in vivo formation of these compounds could be related to the alcohol-abuse syndrome. The basis for this stems from the fact that acetaldehyde is a major metabolite of ethyl alcohol. Plasma concentrations of the acetaldehyde increase following alcohol consumption, thus increasing the likelihood of formation of acetaldehyde-indoleamine condensation reactions. This hypothesis has gained sensational but controversial support from experiments in which rats preferred to drink alcohol over water when tryptolines were injected into their brains.

Our goal in this project is to determine whether any of these compounds are normally present in mammalian tissues and whether their presence is altered by alcohol administration. We have been using the rat as an animal model and have developed reliable assays for measuring the concentration of the serotonin-acetaldehyde condensation product in urine using combined gas chromatography/mass spectrometry.

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RESEARCH PROJECT: BONE DISEASE OF ALCOHOLICS
PROJECT DATES: 1981 -- Present
FINANCIAL SUPPORT: Veterans Administration

DESCRIPTION OF PROJECT:

Subjects with greater than ten (10) years of alcohol abuse are evaluated by serum levels of parathyroid hormone, minerals, and vitamin D metabolites; bone density of the spine is quantitated by CT scan; bone histology is assessed by bone biopsy following double tetracycline labelling. Patients with low turnover osteoporosis are recruited into a therapeutic protocol using Na F.

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Co-principal Investigator

JOHN POLICH, Ph.D.

RESEARCH PROJECT #1: **EVENT-RELATED BRAIN POTENTIALS AND THE INHERITABILITY OF ALCOHOLISM**

PROJECT DATES: 1984 -- Present

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism; J.M. McDonald Foundation

DESCRIPTION OF PROJECT:

The P300 component of the human event-related brain potential (ERP) is being used to study possible differences between individuals with a positive family history for alcoholism compared to individuals without such a history. In addition, the residual effects of alcohol consumption on the P300 potential's amplitude and latency are assessed as a means of ascertaining the neuro-cognitive effects of alcohol consumption in young, social drinkers.

Co-Principal Investigators

CINDY L. EHLERS, PH.D.
STEVEN J. HENRIKSEN, M.D.

RESEARCH PROJECT #2: **CNS EFFECTS OF ALCOHOL: CELLULAR NEUROBIOLOGY**
PROJECT DATES: 12/1/83 - 11/30/87 (current period)
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism (NIAAA)

DESCRIPTION OF PROJECT:

The theme of the Scripps-Salk-UCSD Alcohol Research Center (SSU-ARC) will continue to be organized around the Central Nervous System Effects of Alcohol. The ARC will continue to focus its interdisciplinary molecular, cellular, and behavioral biology methods on the three major subthemes which have emerged from our present research: 1) The molecular and cellular mechanism of short-term alcohol intoxication and its potential endocrine, metabolic and behavioral concomitants (including reinforcing and aversive effects of acute intoxication), 2) The molecular and cellular changes underlying alcohol toxicity to the adult and developing nervous system on chronic exposure; and 3) The molecular, cellular and neuropsychological basis for susceptibility to alcohol dependence and neurotoxicity in humans.The ongoing projects in the SSU ARC are organized into Task Forces focussed on these major subthemes. Individual research components in the ARC are drawn from the Research Institute, and from UCSD, and include the following components: Alcohol Center Core and Administration; Molecular Neuro- pharmacology; Cytochemical Pharmacology; Cellular Neuropharmacology; Systemic Neuropharmacology; Electroencephalography; Behavioral Neuro- biology; Developmental Neurobiology, Molecular and Cellular Neuroendocrinology, Human Evoked Responses, and Molecular and Cellular Biology of the Fetal and Adult Liver

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RESEARCH PROJECT #1: **ADOLESCENT ALCOHOL TREATMENT OUTCOME: RECOVERY PATTERNS**

PROJECT DATES: 8/1986 -- 7/1989

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

Little is known about the rate or process of recovery of adolescents in treatment for alcohol and substance abuse. Although to date comprehensive studies of adolescent treatment outcome have not been completed, clinical accounts suggest that the relapse rates may be even higher than adult populations. The present research project is designed to examine recovery rates for adolescents in treatment for alcohol and substance abuse, and to test whether pretreatment and posttreatment factors predict the rate of success following treatment. Recent evidence from this laboratory indicates that adolescent alcohol abusers are significantly different from demographically comparable nonabusing peers in terms of reinforcement expected from alcohol, stress levels, and strategies employed when coping with drinking pressures. While these factors have been found to relate to treatment outcome in adult alcoholics, their predictive value for adolescents is unknown.

The current study utilizes a longitudinal design which will:

1) Determine relapse rates for adolescents in treatment for alcohol and chemical dependence;

2) Critically examine which pretreatment and posttreatment factors predict outcome for adolescents following inpatient treatment for alcohol and/or chemical dependence; and

3) Test whether potentially modifiable features of adolescent functioning discriminate long-term success from treatment failures.

Participants will be 250 abusing adolescents and their parents (or parental figures) who are 3 weeks into treatment, and at 6 and 12 months following discharge. Levels of functioning in major life areas as well as alcohol and drug consumption will be examined at each point in time.

RESEARCH PROJECT #2: **EXPECTANCIES IN PRIMARY AND SECONDARY ALCOHOL ABUSE**

PROJECT DATES: 10/1985 -- 9/1988

FINANCIAL SUPPORT: Veterans Administration

DESCRIPTION OF PROJECT:

The primary objective of this project is a clarification of the progression of abusive alcohol consumption across medical and psychiatric populations. While diagnoses and etiology may vary across populations, repeated abuse of alcohol may share common developmental features which act to perpetuate or exacerbate the problem. This project focuses on the extent to which alcohol expectancies are related to primary and secondary alcohol abuse and predictive of repeated abusive drinking episodes. The role of expectancies in mediating alcohol consumption is tested by examining the generalizability and specificity of the expectancy-drinking relationship in a three group repeated measures design. It is hypothesized that elevated expectancies of alcohol reinforcement precede acceleration of alcohol consumption and result in a decreased utilization of alternative reinforcers.

Alcoholics in treatment, medical patients and affective disordered patients are studied at three points in time: during hospitalization, and at 3 and 12 months post discharge. At each time the veteran and a resource person are interviewed and complete a variety of standardized questionnaires (e.g., Hamilton Depression Interview, Social Support Questionnaire, Leisure Activity Blank, Situational Confidence Questionnaire). Neuropsychological functioning, affective features,stressful life events, social support, leisure activities, and self-efficacy for alcohol related situations will be examined to assess their relationship with expectancies and impact of the prediction of abuse across populations of primary and secondary alcohol abuse.

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RESEARCH PROJECT: BLACK AND HISPANIC DRINKING PATTERNS
PROJECT DATES: 11/1/84 -- 06/30/87 (current period)
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

This is the first nationwide study in the Black and Hispanic populations of drinking attitudes and patterns, alcohol-related problems, and community attitudes to and experiences with problematic drinking. Interviews will be completed with 1,500 Black and 1,500 Hispanic respondents, in a probability design representative of the adult Black and Hispanic populations of the 48 conterminous states. The study will be coordinated with a nationwide probability sample of the adult U.S. population, supported by an existing National Alcohol Research Center grant. Coordination of the two studies means that findings in the Black and Hispanic populations can be compared with findings in the general adult U.S. population.

The **first objective** of the study is a description of distributions and interrelations in the Black and Hispanic populations of rates of heavy drinking and of alcohol-related problems, of the cultural positioning of alcohol in terms of who may drink how much with whom and in what situations, or norms for and practices by family, friends, and the larger community when drinking behavior become objectionable, and of attitudes and experiences concerning formal interventions by community agencies.

The **second objective** is an analysis, comparing patterns in the Black population, the Hispanic population, and the general White population--with special attention to Whites living in similar circumstances and locations to the Black and Hispanic populations. Preliminary studies suggest that the ethnic differences in rates of heavy drinking and of alcohol-related problems are related to differences by age in duration of heavy drinking, which in turn reflect differences in the cultural norms and sanctions against heavy drinking and problematic drinking.

The **third objective** is an explanatory analysis of patterns of variation within each of the two ethnic study populations. A variety of explanatory factors adduced by the existing literature -- such as acculturation for Mexican-Americans and religiosity for Blacks -- will be measured and analyzed, to test for their potential explanatory power in explaining cultural specificities in Black and Hispanic drinking practices and problems.

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RESEARCH PROJECT: **DEVELOPMENT OF A RAT EVENT-RELATED POTENTIAL MODEL FOR THE STUDY OF ACUTE AND CHRONIC EFFECTS OF ETHANOL**

PROJECT DATES: 12/01/85 - 11/30/87

FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism (NIAA)

DESCRIPTION OF PROJECT:

The goal of the proposed study is to detect and characterize an event-related potential in the rat which could be utilized as a potential marker of both the reinforcing, and neurotixic effects of ethanol. This global objective will be attained by using the following proposed experimental aims.

(1) To develop the appropriate 'rare' stimulus paradigm in order to produce a stimulus bound late wave (>200 msec) which can be successfully averaged from the background EEG.

(2) To test whether low, intoxicating doses of ethanol (<1 g/kg) can alter the latency, amplitude or variability of the rat event-related potential.

(3) To determine whether chronic exposure to ethanol, by the inhalation method, can produce changes in the amplitude or latency of the rat event-related potential and to correlate such changes with behavioral measures of toxicity.

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RESEARCH PROJECT: CALIFORNIA FIRST DUI OFFENDER EVALUATION PROJECT

PROJECT DATES: 01/7/85 -- 01/7/87

FINANCIAL SUPPORT: State of California

DESCRIPTION OF PROJECT: This 24-month project is conducting a comprehensive evaluation of the California First Driving Under the Influence (DUI) offender system. This includes:

1) Identification, development, implementation, and testing of two experimental program models in two counties;

2) A natural variation study of 26 existing programs within a stratified sample of 17 counties;

3) A secondary data analysis of Department of Motor Vehicles (DMV) records to corroborate outcome data and build upon ongoing DMV research; and

4) Management studies in program administrative practices and evaluation/monitoring including the production of two guidebooks for county- and provider-level DUI program managers.

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RESEARACH PROJECT: SYSTEMATIC NEUROPHARMACOLOGY
PROJECT DATES: 12/01/85 - 11/30/87
FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism (NIAAA)

DESCRIPTION OF PROJECT:

The major objective of this component is to investigate possible cellular mechanisms of short-term alcohol intoxication using single-neuron, evoked-potential, electroencephalographic, and behavorial techniques. These efforts will be focused on the norepinephrine-containing nucleus locus coeruleus, a brain system which has the following experimental advantages: 1) it is well-defined anatomically, chemically, and electrophysiologically, so that the possible effects of ethanol can be assessed against a well-characterized set of normative data; 2) the function of this system seems to be a facilitation or refinement of arousal, attention, and information processing capabilities; processes which are profoundly affected by alcohol intoxication; and 3) the neuronal activity of this system seems to be profoundly influenced by intoxicating doses of alcohol. The hypothesis to be tested is that ethanol interferes with the normal functioning of locus coeruleus, an effect that we further hypothesize is partially responsible for the impairment of cognitive functioning caused by intoxication. We propose to test this hypothesis by determining the following: 1) the acute effects of ethanol on locus coeruleus neuron excitability and sensory responses using single-neuron recording in anesthetized rats; 2) the effects of ethanol on spontaneous activity and sensory responses of locus coeruleus neurons in unanesthetized, non-paralyzed rats and squirrel monkeys; 3) the effects, in squirrel monkeys, of acute ethanol administration on event-related potentials which reflect attention and cognitive processing; 4) the interrelationships between ethanol, event-related potentials, and functioning of the locus coeruleus-norepinephrine system; and 5) the effects of ethanol on EEG power spectra and other EEG characteristics in the squirrel monkey.

The efforts of this component are centered on determination of the molecular and cellular mechanisms of short-term alcohol intoxication, and the potential behavioral concomitants of reinforcements and aversiveness. The name, Systemic Neuropharmacology, reflects the attempt of this component to determine cellular responses to ethanol, to describe the behavior of an entire neuronal system under the influence of ethanol, and to then generate an explanation of how this effect on a well-defined neuronal system produces particular changes in behavior or cognition.

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RICHARD CERVANTES, Ph.D.

RESEARCH PROJECT #1: **ALCOHOL EXPECTANCIES AMONG MEXICAN-AMERICAN FEMALE ALCOHOLICS**

PROJECT DATES: 06/1/86 -- 05/30/87

FINANCIAL SUPPORT: Institute of American Studies
University of California

DESCRIPTION OF PROJECT:

The goal of this project, involving 60 Mexican-American women in two recovery homes, is to evaluate the association between alcohol expectancies (measured in Spanish language version of of the Alcohol Expectancies Questionnaire), degree of severity of alcohol involvement (measured by the Diagnostic Interview Schedule (DIS)), and client sociodemographic characteristics.

Co-principal Investigator
RICHARD CERVANTES, Ph.D.

RESEARCH PROJECT #2: **ALCOHOL EXPECTANCIES, ALCOHOL ABUSE, AND ALCOHOL DEPENDENCY AMONG MEXICAN AND MEXICAN-AMERICAN TREATMENT CLIENTS**

PROJECT DATES: 07/1/86 -- 06/30/87

FINANCIAL SUPPORT: University of California Program of Mexico

DESCRIPTION OF PROJECT:

The goal of this project, involving 60 Mexican and Mexican-American women in an outpatient alcohol treatment center, is to evaluate the association between alcohol expectancies, degree of severity of alcohol involvement and client sociodemographic characteristics.

Co-principal Investigator

AMADO M. PADILLA, Ph.D.

RESEARCH PROJECT #3: SCHOLAR IN HISPANIC ALCOHOL STUDIES
PROJECT DATES: 10/1/84 -- 09/30/87
FINANCIAL SUPPORT: National Institute of Alcohol Abuse and and Alcoholism

DESCRIPTION OF PROJECT:

M. Jean Gilbert, a cultural anthropologist with extensive background in the field of alcoholism, has been appointed to fill the position of Scholar in Hispanic Alcohol Studies at the Spanish Speaking Mental Health Research Center. Amado M. Padilla, Ph.D. is Director of the Center. The Scholar will be responsible for the development and implementation of a research program on Hispanic alcohol-related studies. The position will involve two major directions:

1) Research, and
2) Dissemination.

In terms of the research direction the Scholar will employ the conceptual framework of life stress-illness and coping currently guiding the research directives of the Spanish Speaking Mental Health Research Center (SSMHRC). Adhering to this conceptual framework, the Scholar will focus on within-Mexican-American group variation in drinking practices, attitudes, and problems related to alcohol. In addition, attention will be directed to gender and age differences in acculturation and stress, and the relationship of these variables to drinking practices. Other research to be conducted by the Scholar will involve several data bases that will be made available to the SSMRHC for primary and secondary analyses.

With respect to the dissemination function, the Scholar will be responsible for preparing critical reviews of the Hispanic alcohol literature and coordinating seminars and conferences on Hispanic alcoholism. Researchers and service providers will be invited to present their work, and to explore treatment approaches and research examining the relationships of different variables to Hispanic drinking practices.

The Scholar will also work with SSMHRC staff to organize larger scale conferences on such themes as the ethnic and cultural factors involved in the etiology and epidemiology of alcoholism. Central to these activities will be preparation of materials for dissemination of workers in the field of Hispanic alcoholism. Finally, the Scholar will provide technical assistance to researchers and service providers in the development of research on the treatment approaches to Mexican-Americans.

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IVAN DIAMOND, M.D., Ph.D.

RESEARCH PROJECT #1: CHRONIC EFFECTS OF ETHANOL ON NEURAL CELLS IN CULTURE

PROJECT DATES: 05/1/85 -- 04/30/89

FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The physiological effects of EtOH appear to be due to its interaction with the cell membrane. Chronic exposure to EtOH induces changes in the membrane which lead to resistance to the effects of EtOH. However, controversy exists about the actual molecular changes occurring in the membrane which result in such tolerance to EtOH. We are studying neuronal cells in culture as a model system to determine the molecular mechanisms underlying the long-term changes after exposure to EtOH. We are using membrane enzymes which we can assay in intact, living cells to determine the time course for development of these changes. Since we use a homogeneous cell line in a defined medium where changes in EtOH concentration are the only variable, we will be able to observe changes in membrane function and lipid composition due to chronic treatment with EtOH. Moreover, since membrane lipid composition can be altered by changing the medium in which the cells grow, we will be able to selectively change membrane lipids and determine the role of individual lipids in the development of tolerance by altering membrane lipid composition.

Co-principal Investigator

IVAN DIAMOND, M.D., Ph.D.

RESEARCH PROJECT #2: **ETHANOL TOLERANCE AND DEPENDENCE AT A CELLULAR LEVEL**

PROJECT DATES: 01/1/86 -- 12/31/86

FINANCIAL SUPPORT: Alcoholic Beverage Medical Research Foundation

DESCRIPTION OF PROJECT:

The physiologic effects of ethanol appear to be due to its interaction with the cell membrane. Chronic exposure to ethanol induces changes in the membrane which probably account for tolerance and physical dependence. However, it is difficult to apply this information to patients. We have established a model neuronal cell culture system in which adenosine receptor-dependent cAMP levels are stimulated by ethanol added acutely but become tolerant to this effect in vitro after chronic exposure to ethanol. Tolerance is characterized by reduced receptor-dependent cAMP levels and ethanol added acutely now restores levels to normal values. The same receptor-coupled system occurs in human lymphocytes and we have found that chronic alcoholic lymphocytes show depressed basal and stimulated cAMP levels when compared to normal subjects and patients with liver disease. We plan to determine whether alcoholic lymphocytes recover after alcohol withdrawal and during detoxification. We also plan to study whether lymphocytes from alcoholics show abnormal adaptive mechanisms to ethanol when incubated in vitro. We know that changes in the cell culture medium can determine whether or not cells adapt to the presence of ethanol. We plan to determine the role of individual phospholipids, fatty acids, and cholesterol in the development of cellular tolerance to ethanol. We will try to exaggerate or prevent this adaptive response so that we can design specific therapies to prevent or treat alcoholism in patients.

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RESEARCH PROJECT: ROLE OF ALCOHOL WITHDRAWAL IN ALCOHOLISM OUTCOME

PROJECT DATES: 08/01/85 -- 07/31/88

FINANCIAL SUPPORT: National Institute on Alcoholism Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The objective of this study is to characterize the symptomatology and time course of the alcohol withdrawal syndromes (acute, subacute, chronic), and to determine the influence of withdrawal severity and duration on long-term drinking behavior and psychiatric and social status. An unselected series of 100 male alcoholic patients will be followed for one year after being admitted to a four-week inpatient alcoholism treatment program within 24 hours of their last drink. Severity of withdrawal, psychological and somatic distress (Hopkins SCL-58), anxiety, depression (Beck Depression Inventory, Hamilton Depression Scale), desire to drink alcohol (visual-analogue scale), and self-reported drinking history will be assessed weekly as an inpatient, then after 3, 6, 9, and 12 months of follow-up. Psychosocial status at baseline and after follow up will be assessed using structured interviews (Diagnostic Interview Schedule and Addiction Severity Index). These data may suggest clinical variables predictive of relapse to drinking or psychosocial problems requiring attention. Knowledge of such variables would improve the effectiveness and efficiency of alcoholism treatment.

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RESEARCH PROJECT: **INTERACTIONS OF ETHANOL AND RELATED DRUGS WITH ION CHANNELS AND NEUROTRANSMITTER RECEPTORS**

PROJECT DATES: 07/1/82 -- 06/30/90

FINANCIAL SUPPORT: Alfred P. Sloan Foundation, Alcoholic Beverage Medical Research Foundation -- National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

Effects of ethanol on neurotransmitter receptor binding and ion flux are studied in brain membranes and cultural neural cell lines. We are particularly interested in interactions of ethanol and other drugs with the GABA-benzodiazepine-chloride channel complex and the voltage-gated calcium channel. Current projects include studies of calcium channel inactivation, anticonvulsant inhibition of calcium flux, mechanisms of action of calcium channel 'agonist' drugs, and photoaffinity labeling of receptors and ion channels.

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RESEARCH PROJECT: **FOLATE METABOLISM IN THE ALCOHOLIC PIG**
PROJECT DATES: 04/1/86 -- 03/31/89
FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The objective of the study is to define mechanisms of malnutrition in chronic alcoholism. The miniature pig is used as our experimental model, since this animal drinks alcohol ad libitum. Beer with added ethanol is provided daily, with the objective of achieving daily intakes of 3-4 g ethanol per kg body weight. We are particularly interested in folate metabolism, since deficiency of this vitamin is the most common sign of malnutrition in chronic alcoholism. The project will include studies of intestinal absorption of radioactive folates, which will be introduced through permanently implanted intestinal canulas, studies of intestinal folate enzymes, studies of the excretion of radioactive folates in the bile, and studies of the metabolism of folates in the liver. The pigs (5 fed alcohol and 5 control) are housed in the Animal Resource Service of the University of California, Davis, under conditions which have been approved by the Animal Welfare Committee of the University of California, Davis, and by the National Institutes of Health. The pigs will also be used to study the effect of chronic alcoholism on nutrition, in particular as related to the pathogenesis of alcoholic liver disease.

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RESEARCH PROJECT: ADOLESCENT ALCOHOL PREVENTION TRIAL (AAPT)
PROJECT DATES: 03/01/84 -- 02/29/1994
FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

This research addresses two unresolved issues which have emerged from previous studies on alcohol abuse prevention. The first issue involves an examination of programs to test competing theories of why social psychological programs may be successful. The second issue concerns the age at which programs may be effective for reducing alcohol abuse among adolescents. The aims of this research are to:

1) Reduce the incidence and prevalence of alcohol abuse among adolescents;
2) Test the relative efficacy of social psychologically based prevention programs which focus on social influence resistance training versus normative education versus a combined approach;
3) Test the efficacy of prevention programs which are delivered at seventh versus ninth grades.

This is a five year project and is divided into two phases:

Phase I (now completed)--Materials were refined and process evaluation was the focus on research activities. Preliminary findings suggest that receiving the resistance training program led to greater knowledge of social sources of pressure to use alcohol, whereas, receiving a normative expectations curriculum led to a greater awareness of conservative norms within schools. Students who received only information about consequences of use showed a greater knowledge of the consequences of drinking. Comparability of programs in terms of peer leader involvement and health educator delivery of programs will be assured via empirical tests of these on founding variables.

Phase II--Will involve a formal test of the three curricula as preventative treatments for seventh and ninth grade students. Junior-senior high school complexes will be randomly assigned to receive a resistance training, normative education, or combined program, each of which focuses on preventing the onset of alcohol abuse. All programs use same-age peer leaders as program facilitators. Subjects will be pre- and post-tested with a questionnaire assessing alcohol use, attitudes, beliefs, normative expectations, self-efficacy, and use by others. Special attention will be devoted to assessing variables hypothesized to mediate program effectiveness.

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RESEARCH PROJECT: POST-DISQUALIFICATION CONTROL OF DUI OFFENDERS
PROJECT DATES: 10/1/85 -- 09/30/88
FINANCIAL SUPPORT: California Office of Traffic Safety

DESCRIPTION OF PROJECT:

This project will involve the development and evaluation of traffic safety countermeasures targeting the suspended/revoked DUI offender and other high risk drivers who continue to drive while disqualified. A sample of disqualified drivers will be identified from DMV records for descriptive and prior driver record analyses and a portion of these disqualified drivers with driver record entries during the period of disqualification will be tracked back through the adjudicating court to isolate the process and system deficiencies underlying failure to convict for CVC 14601. Countermeasures designed to increase the identification, prosecution, and conviction of those who drive while disqualified will be developed, implemented in demonstration areas, and evaluated.

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RESEARCH PROJECT #1: **CONTRA COSTA COUNTY GENERAL POPULATION SURVEY**
PROJECT DATES: 02/87 -- 02/88
FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

A general population survey of 3,000 adults in Contra Costa County will examine drinking patterns, drinking problems and the community response to drinking patterns with special emphasis on the process through which problem drinkers are extruded out of the community into treatment.

RESEARCH PROJECT #2: **THE EPIDEMIOLOGY OF DRINKING PROBLEMS: ANALYSIS OF THE 1984 NATIONAL ALCOHOL SURVEY**
PROJECT DATES: 01/1/86 -- 01/1/87
FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

This work consists of a series of papers emanating from the analysis of the 1984 National Alcohol Survey data set. These data were gathered from a nationwide probability sample of over 5,000 respondents. My work revolves chiefly around analyses of the epidemiology of drinking problems within these data.

The current paper in this series is a multivariate analysis of the relationships between drinking patterns, and selected demographic variables. The demographic distributions of drinking problems in the U.S. population are well-known, having been documented in a number of studies. These problems are more prevalent among those who are male, young, single, residents of the wet regions of the county, urbanites, less educated, and of lower socioeconomic status. Not surprisingly, these distributions of drinking problems match the distributions of heavy drinking, which have also been well studied. However, few studies have attempted to find out whether demographic variables are associated with a higher risk of drinking problem after controlling for alcohol intake. This research conducts such an analysis by constructing multivariate models in which drinking problem scores are predicted on the basis of the frequency of heavy drinking occasions, sex, age, marital status, region, urbanization, income, and education. The results indicate that these variables have little association with the reported problem level at a given frequency of heavy drinking occasions.

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RESEARCH PROJECT: **ENVIRONMENTAL APPROACHES TO PREVENTION**
PROJECT DATES: 10/1/83 -- 11/30/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The purpose of the Prevention Research Center is to develop, evaluate, and disseminate innovative approaches to the prevention of alcohol-related problems. The focus of the Center is environmental, and thus represents a significant shift away from efforts to change the habits of the individual drinker. The model from which the Center's program of research derives stresses the importance of such factors as server practices, local, state and federal policies and laws, economic fluctuations, and media portrayals of alcohol in the etiology of alcohol-related problems.

The program of research is organized into five components. Each component addresses a different aspect of the drinking environment.

Component I is a quasi-experimental evaluation of server intervention programs on naval bases and in college fraternities.

Component II assesses the impact of minimum drinking age changes and economic fluctuations on alcohol-related traffic crashes using secondary data analysis.

Component III is a national survey to study the nature and implementation of high school alcohol policies.

Component IV expands a complex family-level cultural model of alcoholism through anthropological study of high-risk families, and will assess the model's potential application to prevention.

Component V focuses on alcohol and mass media including annual content analysis of prime-time television and a biannual analysis of college newspapers.

To carry out the Center's extensive program of research, a multi-disciplinary team of scientists has been assembled. These individuals represent academic and professional perspectives from public health, sociology, planning, anthropology, communications, psychology, education, law, and information sciences.

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RESEARCH PROJECT: ALCOHOL CONSUMPTION AND MULTIPHASIC HEALTH EXAMINATION FINDINGS

PROJECT DATES: 07/1/85 -- 06/30/87

FINANCIAL SUPPORT: Alcohol Beverage Medical Research Foundation
John Hopkins University

DESCRIPTION OF PROJECT:

This is an epidemiologic study of alcoholic beverage consumption and health in a large population. Alcohol habits are determined by questionnaire responses at health examinations. Since 1978 a new research alcohol questionnaire has been completed by more than 120,000 different persons. It provides a lifetime alcohol history, information about the entire range of alcohol use, information about beverage types, tables, and demographic data. This is used to study relations of alcoholic beverage use to other baseline health measurements. Underway is a long-term prospective follow-up of this large cohort to examine such outcomes as hospitalizations and mortality.

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RESEARCH PROJECT: BEHAVIORAL PHARMACOLOGY
PROJECT DATES: 12/01/85 - 11/30/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism (NIAAA)

DESCRIPTION OF PROJECT:

This component utilizes a wide variety of behavioral and neurosurgical methods to examine the basis of acute, chronic and neurotoxic effects of alcohol. Three general behavioral methods are proposed to assess the mechanisms underlying ethanol addictive phenomena and human alcoholism. 1) Studies are planned to extend current research and explore the intoxicating mechanisms of alcohol response, focusing on the acute ataxic and anxiolytic effects of ethanol using an operant multiple schedule modification of the Geller-Seifter conflict test. An attempt will be made to distinguish between these two separate effects of ethanol using behavioral tolerance, pharmacology and specific neurochemical lesions to analyze for particular neurotransmitter involvement. 2) Previous studies of chronic ethanol exposure will be extended to complete the characterization of the necessary conditions and neurochemical mechanisms for ethanol self-administration in rats. Rats chronically exposed to different concentrations of ethanol in the Scripps Alcohol Research Center ethanol vapor chambers will be tested for intragastric self-administation of ethanol. The minimum chronic blood-ethanol level necessary to establish and maintain self-administration after defined periods of chronic exposure will be determined. Drugs, neuropeptides, and specific neurochemical lesions will be used to attempt to modify this dependence in order to determine its mechanism. 3) A model system will be developed to determine neurotoxic effects of chronic ethanol exposure. Treatments will include chronic high ethanol vapor exposure and ethanol vapor exposure combined with dietary vitamin (thiamine) restriction; the initial measure of neurotoxicity will center on general tests of "memory" impairment, e.g., active and passive avoidance; spatial discrimination, and delayed response paradigms. Emphasis will be placed on the development and indentification of behavioral tests sensitive to the neurotoxic effects of chronic ethanol exposure with the ultimate aim of discovering the mehanism of action of ethanol and the potential for development of useful therapeutic agents to prevent ethanol-induced neurotixicity. These studies will clarify the anatomical and neurochemical basis for the addictive effects of chronic alcohol exposure, clarify the basis for interindividual susceptibility to these addictive effects, as well as seek to develop behavioral tests which will provide insight into the basis of neurotoxic effects of alcohol.

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RESEARCH PROJECT: **REANALYSIS OF THE SAN FRANCISCO BLACK DRINKING PRACTICES STUDY DATA**

PROJECT DATES: 09/1/85 -- 07/30/87

FINANCIAL SUPPORT: Self and the California Department of Alcohol and Drug Programs

DESCRIPTION OF PROJECT:

Data from the 1979-1981 San Francisco-based Black Drinking Practices Study are being used to test whether the results of the ethnographic research methodology are comparable to those of a general population survey. Both research methodologies were used during the original study.

Over 100 ethnographic findings are being compared with responses from a 53-page household survey of 423 Black adults regarding their drinking practices and opinions on the use of alcohol.

Indepth analyses of the data are underway, with the results being compared with those from prior and more recent studies. Data are being analyzed by level of drinking and alcohol problems; demographic characteristics of age, sex, religious practices and recreational drug use; and attitudes towards alcohol use and alcoholism treatment.

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RESEARCH PROJECT: PRENATAL ALCOHOL: ENDROCRINE AND SEXUALLY DIMORPHIC EFFECTS

PROJECT DATES: 01/1/85 -- 12/31/87

FINANCIAL SUPPORT: National Institutes of Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

Acute and chronic ethanol administration is known to affect circulating levels of gonadal hormones in adult animals and humans. Since alteration in these hormone levels during the perinatal period can have profound long-term consequences on adult expression of sexually dimorphic behaviors and neuroendocrine function, it is important to determine whether such alterations exist in animals exposed prenatally to ethanol. Preliminary studies suggest that such changes are present in adult animals exposed to ethanol in utero during the last trimester of pregnancy. The studies in this proposal have been designed to integrate both behavioral and endocrinological measures to determine whether the changes which we have observed are associated with ethanol-induced alterations in circulating levels of steroid hormones during the prenatal period. Moreover, the studies are designed to assess whether these long-term changes are due to an effect of ethanol on the organizations or activational aspects of the physiology underlying the adult expression of sexually dimorphic behaviors. The results of these experiments may lead to more efficacious strategies for the treatment of children of alcoholic mothers.

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RESEARCH PROJECT: **SOBRIETY MAINTENANCE AMONG SIOUX (LAKOTA) INDIANS: GENDER DIFFERENCES IN DRINKING STYLES AMONG NATIVES (PLAINS GROUPS)**

PROJECT DATES: 1969 -- Present

FINANCIAL SUPPORT: Self

DESCRIPTION OF PROJECT:

The major study has been accepted for publication and deals with an ethnography of drinking and sobriety among the Lakota (Sioux) Indians. Since impressionistic studies of gender differences are emerging, the present orientation is to document and discuss the actualities of the drinking experience across gender lines.

Co-Principal Investigator

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DR. J. H. MORRISON

RESEARCH PROJECT: THE EFFECTS OF ETHANOL ON BRAIN DEVELOPMENT
PROJECT DATES: 12/01/85 - 11/30/87

FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism (NIAAA)

DESCRIPTION OF PROJECT:

The development of the central nervous system is a complex process involving cell division, migration, differentiation and cell death. Disruption of these processes by ethanol in utero in humans can lead to the condition known as fetal alcohol syndrome, defined by a particular pattern of anatomical malformations, their unknown cellular consequences and, ultimately, mental retardation. Animal model studies from this and other laboratories have indicated specific neurochemical and neuroanatomical abnormalities in neonates exposed to ethanol in utero. These studies, however, have not been sufficiently comprehensive to distinguish whether ethanol exposure has general effects, for example, on gene expression or peptide processing, or whether it specifically disrupts the development of particular functional systems. To examine these questions we propose to investigate the developmental expression of several different brain gene products in normal rats and rats treated with ethanol in utero.

These studies will utilize the rat model system for prenatal ethanol exposure previously and extensively defined in this Alcohol Research Center and will emphasize two directions of investigation:

1) The extension of the previous biochemical findings demonstrating changes in peptide levels in ethanol exposed neonates to the immunohistochemical localization of well-defined neuropeptide systems, with particular attention to possible effects on differential processing of their precursors.

2) A survey for potential disruptions in gene expression using specific probes for the mRNA and protein products of defined brain specific genes.

Together these two approaches will initiate a two-year pilot project to evaluate the degree to which these strategies can clarify the effects of ethanol on the expression of a wide variety of brain gene products from the gene to the final functional protein or peptide product.

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RESEARCH PROJECT #1: **EVALUATING ALCOHOLISM-INDUCING COMMUNITY SETTINGS**

PROJECT DATES: 06/1/76 -- 08/31/87

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism, Veterans Administration

DESCRIPTION OF PROJECT:

This research program has five major aims:

1) Develop a new conceptual approach to evaluating alcoholism treatment programs. This approach incorporates information about the treatment environment to which the patient is exposed, the actual treatment experiences that patients under go, and work and family settings that may facilitate favorable treatment outcome;

2) Develop new ways of measuring social environments to identify the salient dimension of the community setting in which alcoholic patients function;

3) Compare families with an alcoholic patient with normal-drinking control families to assess the role of family, work, and community settings in drinking behavior;

4) Compare persons entering and not entering treatment after contacting a detoxification or alcoholism information/referral center. This comparison should shed light on the determinants of treatment entry, the effects of treatment, and the processes of recovery and relapse among treated and untreated alcoholics; and

5) Investigate the clinical utility of giving alcoholic patients and their families systemic feedback regarding their family environments.

We hope to develop techniques whereby information about patients' environments can be systematically used in clinical case descriptions and in overall treatment planning.

RESEARCH PROJECT #2: **LIFE STRESSORS AND PROBLEM DRINKING AMONG OLDER ADULTS**

PROJECT DATES: 08/1/85 -- 07/31/89

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism, Veterans Administration

DESCRIPTION OF PROJECT:

This project examines the influence of life stressors, coping responses, and personal and social resources on the drinking behavior of persons 60 and older. A large sample of older persons is being screened to identify those with current drinking problems, those "at risk" to develop such problems, and those with few risk factors. These smaller groups will be studied over a one-year period to explore the cross-sectional and longitudinal relationships of stressors to drinking behavior and other areas of functioning (e.g., depression) and the extent to which personal resources and coping responses, along with social resources (e.g., social support), mediate and/or moderate the effect of stressors on functioning. The study employs a recently-developed instrument that assesses stressors and resources in the same life areas (e.g., financial matters, marital relationship), and a new measure of coping responses and cognitive appraisal. The project should illuminate some of the processes involved in the development of (new episodes of) problem drinking among older persons.

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Co-Principal Investigator

Victor Coleman, J.D.

RESEARCH PROJECT #1: **COMMUNITY GUIDE TO ALCOHOL AVAILABILITY LAWS AND REGULATIONS**
PROJECT DATES: 06/25/86 -- 06/24/87
FINANCIAL SUPPORT: California Department of Alcohol and Drug Programs

DESCRIPTION OF PROJECT:

To provide guidance for community members and organizations to become involved in California Department of Alcoholic Beverage Control licensing and enforcement proceedings by developing and distributing a handbook that will explain the opportunities available to localities regarding alcohol availability in their communities.

Co-principal Investigator

ROBERT ROTH, J.D.

RESEARCH PROJECT #2: **PREVENTION RESEARCH: ABC POLICIES ON DRUNK DRIVING**
PROJECT DATES: 4/86 -- 9/88
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The project is a descriptive study which focuses on the role of Alcoholic Beverage Control (ABC) agencies in preventing drinking driving. ABC agencies have the authority and responsibility to regulate the business practices of retailers of alcoholic beverages and to determine the number and location of retail outlets. ABC's are therefore key actors in comprehensive server intervention programs which involve actions taken by commercial servers to reduce the likelihood that those being served will harm themselves or others.

Research will include collection of secondary source data regarding the structure and mandates for ABC agencies in all 50 states and the District of Columbia. There will also be more detailed studies of selected state ABC's which are notable for unique programs or major changes in mandated activities.

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RESEARCH PROJECT: **SURVEY OF HIGH SCHOOL ALCOHOL POLICIES**
PROJECT DATES: 04/1/84 -- 03/31/86
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The high school alcohol policy study is a descriptive study of student alcohol and drug use policies in the United States. The study assesses the nature and prevalence of such policies and explores the relationship between the type of school policy and characteristics of the school, its staff, and students. The extent to which school policies differentiate between alcohol and drug violations and the manner in which such violations are handled will be examined. A methodology of assessing the impact of school policy on student alcohol and drug use will be developed. The study will offer recommendations for effective high school policy.

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RESEARCH PROJECT: COLLEGE STUDENT DRINKING STUDY
PROJECT DATES: -- Ongoing --
FINANCIAL SUPPORT: Currently not funded, but work is proceeding

DESCRIPTION OF PROJECT:

Survey of the drinking behavior of a probability sample of over 2,000 students from nine university campuses in three sites on the West Coast. Trends in quantity and frequency of drinking are assessed for two campuses first studied in 1979 with a second rate point from 1981.

In addition to trends in drinking behavior on the two campuses, data from all nine campuses are used to describe variations in student drinking behavior and experiences. Particular emphasis is placed on identification of the times and places, the social contexts and reasons students give for drinking.

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Co-Principal Investigators

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RESEARCH PROJECT: HUMAN EVOKED RESPONSES
PROJECT DATES: 12/01/85 - 11/30/87
FINANCIAL SUPPORT: National Institute on alcohol Abuse and Alcoholism (NIAAA)

DESCRIPTION OF PROJECTS:

Our broad goals are to investigate the mechanisms whereby acute and chronic ethanol ingestion affect sensory and cognitive functions and related neural systems in humans. We employ converging behavioral and electrophysiological event-related potential measures in paradigms designed to reliably assess the integrity of brain systems related to senory, attentional, mnemonic and semantic functioning. Specifically, on the basis of our research, we propose five series of studies: I. Investigate the hypothesis that naloxone may reverse some of ethanol's acute effects on sensori-neural, attentional and/or mnemonic functioning and related brain systems. II. Assess the effects of chronic ethanol abuse on sensory and cognitive processes in paradigms which permit the separate assessment of sensory, attentional, encoding, retrieval, and storage functions. III. Develop paradigms with which to assess perceptual and neural development in infants and children so that we can determine the degree of maternal ethanol consumption which may place infants at risk in terms of cognitive and neural maturation. IV. Replicate and extend our recent results which suggest that ethanol affects brain functions differently in individuals with and without a positive family history for alcoholism. We will further explore the possibility that these groups of individuals, who are at high and low risk, respectively, for developing alcoholism, may be differentiated on some measure of cognitive and brain functioning even without a challenge of ethanol. V. We will develop models of human event-related potentials in the squirrel monkey in order to determine the neural structures and systems which generate ethanol sensitive event-related potential components.

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Co-principal Investigator

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NANCY BRILL, M.D.

RESEARCH PROJECT1: DEVELOPMENT OF INFANTS WHOSE MOTHERS DRINK
PROJECT DATES: 1/1/81 -- 1/1/87
FINANCIAL SUPPORT: Not Stated

DESCRIPTION OF PROJECT:

The purpose of the research is to study the relation between alcohol use in elderly primiparous mothers and one-year infant development. Our objectives are to study the association between maternal alcohol use and infant morphogenesis, cognition, and social/emotional development. Mother-infant dyads were studied when the infant reached 12 months of age. Maternal alcohol use was evaluated using self-report questionnaires developed by Streissguth, Martin and Buffington (1977) based upon the measures of Jessor (1968) and Cahalan (1969). Infants were evaluated for abnormalities of morphogenesis during physical examination. Particular attention was paid to major and minor physical anomalies ascribed to fetal alcohol syndrome. The Bayley Scales of Infant Development served as the measure of infant cognitive development. Infant social/emotional development was determined by the quality of the infant's attachment behavior as measured by the Ainsworth Strante-Situation paradigm.

Eighty percent (80%) of the children whose mothers claimed to have consumed 5 or more drinks on any one occasion during pregnancy had physical anomalies in contrast to only 8 percent (8%) of the children of mothers who consumed two or less drinks at any time during pregnancy. A significant linear relation between infant mental development and drinking prior to pregnancy was found. The average mental development score of infants whose mothers consumed two drinks a day or more was 95 in contrast to a score of 115 in infants whose mothers consumed less than 1/4 of a drink a day. With regard to social/emotional development, mothers of infants found to be securely attached drank significantly less than mothers of insecure infants. Furthermore, 92 percent (92%) of infants whose mothers consumed more than 2 drinks per day were judged insecurely attached in comparison to 20 percent (20%) of infants whose mothers were abstinent or light drinkers. No alcohol measures were significantly correlated with condition of birth, postnatal illness, or growth parameters at birth and at one year.

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RESEARCH PROJECT: DISTANT REGULATORY GENES IN DROSOPHILA, STUDIES OF MAMMALIAN GENE REGULATION

PROJECT DATES: 12/01/83 -- 03/31/87

FINANCIAL SUPPORT: National Institute on Alcoholism and Alcohol Abuse -- National Institute on Health

DESCRIPTION OF PROJECT:

Distant regulatory genes, which are not closely linked to the structural gene they regulate and so presumably send diffusible molecular regulatory signals, are poorly understood in higher eukaryotes. Our goal is to identify a set of such regulatory loci controlling alcohol dehydrogenase expression in Drosophila and to characterize these for their location, tissue specificity of action, and molecular level of function.

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RESEARCH PROJECT: ALCOHOL USE AND PHYSICAL HEALTH
PROJECT DATES: Indefinite
FINANCIAL SUPPORT: California State University Grant

DESCRIPTION OF PROJECT:

Examination of alcohol use and other health practices on facets of physical health in several data sets from general population surveys.

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RESEARCH PROJECT:	**CNS DEFICITS: INTERACTION OF AGE AND ALCOHOLISM**
PROJECT DATES:	07/1/86 -- 06/30/91
FINANCIAL SUPPORT:	National Institute on Alcohol Abuse and Alcoholism, Veterans Administration

DESCRIPTION OF PROJECT:

The continuation of this project will use an age-regression model to confirm that, in chronic alcoholics, certain electrophysiological, cognitive, and brain structural variables show evidence of central nervous system (CNS) deficits beyond age norms. The role of age, alcohol exposure, nutritional status, and family history of alcoholism in these deficits will be tested. The phenomenon of reversibility will be investigated and factors contributing to it evaluated.

The specific CNS variables to be measured include:

1) Amplitude latency and topographic distribution of the P300, a cognitive component of the event-related potential (ERP);

2) Performance on neuropsychological tests of concept formation, visuo-spatial abilities, and memory (standardized against estimates of premorbid general intelligence);

3) Brain atrophy, quantified by measuring the proportion of cerebrospinal fluid (CSF), white matter and grey matter at anatomic regions of interest such as ventricles and cortical sulci visualized by Magnetic Resonance (MR) imaging; and

4) Brain tissue hydration, quantified by deriving T1 and T2 values for whole brain sections imaged by MR, and measuring mean values within designated regions of interest.

Chronic alcoholics ranging in age from 25 to 65 will be tested during the first and fourth week of withdrawal and after an interval of 12 months. Healthy community volunteers across the same age range, will also be tested at equivalent intervals. Cross-sectional analyses will determine the extent to which alcoholics can be shown to have CNS deficits over and above those expected for their age. Within-group analysis will relate specific subject characteristics such as nutritional status, exposure to ethanol, family history of alcoholism, and age, to these CNS deficits. Longitudinal analysis will determine the extent to which deficits, including brain atrophy, are reversible during a three-week period of abstinence, and what further changes are seen after one year.

Co-principal Investigators

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MARY JANKE, Ph.D.

RESEARCH PROJECT: **DEVELOPMENT OF AN IMPROVED MANAGEMENT CONTROL SYSTEM FOR DUI DRIVERS**

PROJECT DATES: 04/86 -- 03/87

FINANCIAL SUPPORT: Office of Traffic Safety

DESCRIPTION OF PROJECT:

The project is designed to develop the framework for an optimum DUI control system based on the principal of systems analysis. The system model will include statement of system and subsystem goals, system and subsystem objectives, and a management information system to provide annual "State of the System" reports.

The report will produce the detailed specifications and report formats for a management information system.

Co-principal Investigators

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WYLIE VALE, Ph.D.
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RESEARCH PROJECT: NEUROENDROCRINE EFFECTS OF ETHANOL
PROJECT DATES: 12/01/77 -- 11/30/87
FINANCIAL SUPPORT: National Institute of Health

DESCRIPTION OF PROJECT:

Study of the effects of ethanol (E) on various parameters of endocrine and CNC functions. In particular, we establish or extend information on the acute and/or chronic effects of E on the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-gonadal (HPG) axis; study the initial site of E's action on these systems, with particular emphasis on the hypothalamic peptide components, investigate the possible interaction of factors such as stress in the E effects; probe the roles of stress modulating peptides such as corticotropin-releasing factor in the effects of E and stress.

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RESEARCH PROJECT: **MENTAL HEALTH CLIENT STUDY: PART OF THE COMMUNITY LABORATORY PROJECT**

PROJECT DATES: 12/1/85 -- 12/1/90

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The study of clients with alcohol involvement in mental health treatment facilities addresses both broad and specific research concerns. The broad concerns include:

1) Pathways to treatment;

2) Linkages among agencies and agency ecology;

3) A cataloguing of events which extrude individuals from the general population into the treatment population(s);

4) A description of the goals, priorities, and orientations of treatment providers in both alcohol and nonalcohol specific agencies; and

5) A sustained attention towards detailing formal and informal mechanisms of community response to alcohol-related problems, including parameters of acceptability and rejection of alcohol-related behavior as defined by the general population.

Specific concerns of the mental health study include:

1) A description of the range of alcohol involvement among client problems in mental health treatment facilities;

2) A documentation of events which trigger clients(s) entry into treatment and, where possible, a discernment of why clients with alcohol-related problems have become a part of the mental health client population as opposed to becoming a part of alcohol specific agency populations;

3) A description of public and private dimensions and referral patterns within the mental health system county-wide; and

4) An historical documentation of social views regarding alcoholism and mental health as they relate to : diagnostic categories; stigma and destigmatization; the proliferation and changing face(s) of treatment/support agencies; social and financial policies; and a characterization of clients and their alcohol-related problems, over time as they relate to community responses.

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RESEARCH PROJECT: **EPIDEMIOLOGY OF ALCOHOL PROBLEMS**
PROJECT DATES: 12/1/85 -- 11/30/90
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism, Alcohol Research Center Grant

DESCRIPTION OF PROJECT:

As a National Alcohol Research Center, the Alcohol Research Group's (ARG) focus is on the Epidemiology of Alcohol Problems. Research performed under the Center grant from the National Institute on Alcohol Abuse and Alcoholism is coordinated with other research support from public sources. From a central base in survey research on drinking practices and problems, ARG's research program has broadened to encompass a variety of research tools and methods, and to include legal, historical, policy , and conceptual analysis of the definition and patterning of alcohol problems in human populations. In broad terms, the common objective of the studies is a greater understanding of the place of drinking patterns and problems in society. The emphasis is on naturalistic data--on the study of drinking patterns and problems as they occur in the course of everyday life, whatever the specific methodology employed. Attention is paid to institutional and collective definitions and responses as well as to individual attitudes and behaviors.

The specific current projects of the Center are listed separately in this compilation. In addition to these ongoing major research projects, the Center grant supports a variety of activities in which the Alcohol Research Group acts as a nexus for social and epidemiological alcohol research. The Group publishes The Drinking and Drug Practices Surveyor as a medium of international communication among researchers, and members of the Group have coordinated the Alcohol Epidemiology Section of the International Council on Addictions, chaired the Association of Substance Abuse Librarians and Information Specialists, organized the alcohol and drug studies program at meetings of the American Public Health Association, the American Anthropological Association, and the American Sociological Association, edited topical issues of such journals as The Journal of Drug Issues and Contemporary Drug Problems and served on a variety of regional, national, and international study groups and advisory bodies.

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RESEARCH PROJECT: SERVER INTERVENTION PROJECT
PROJECT DATES: 10/1/83 -- 11/30/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The Server Intervention Project measures the efficacy of server intervention for reducing a variety of problems associated with drinking in public settings. The Project is designed to estimate the program's impact in a specific, relatively well-controlled environment (a military base), through the use of a nonequivalent control group design. The research comprises four phases:

1) To identify and collect baseline data on current server practices, drinking behavior and problems associated with drinking;

2) To adapt, refine, and implement a server training program;

3) To evaluate training effectiveness in changing servers' behavior; and

4) To use the variables defined in Phase 1, to measure the impact of server intervention on drinking behavior and associated problems.

The project is currently in the fourth phase.

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RESEARCH PROJECT #1: CENTER FOR CLINICAL RESEARCH IN ALCOHOLISM
PROJECT DATES: 04/1/85 -- 03/31/90
FINANCIAL SUPPORT: Veterans Administration

DESCRIPTION OF PROJECT:

The Center is a collaboration by the departments of psychiatry, psychology, laboratory medicine, medicine, nuclear medicine, and the nursing service to enhance our understanding of clinical aspects of alcoholism at our Veterans Administration Medical Center. We propose to create a series of Core resources to:

1) Be shared by scientists of different disciplines;

2) Maximize the probability that young scientists will conduct successful alcoholism research projects through their interactions with more established investigators; and

3) Encourage more senior scientists who have worked peripherally in the alcohol area to initiate more research in clinical aspects of alcoholism.

The Center for Clinical Research in Alcoholism will maximize productivity and efficient sharing or resources by screening and assigning potential subjects to research protocols, collecting baseline and follow-up information for multiple studies, and creating a data bank on all participating patients to be shared by Center scientists. The Core will also enable the individual research projects to exchange information, thereby enhancing the quality of investigations.

All primary alcoholics and primary affective disorder secondary alcoholics entering the ATP inpatient program will be asked to participate in a structured interview covering their own alcohol history, history of other psychiatric and drug problems, and family history of similar disorders. In addition, a first-degree relative will also be interviewed. Patients will undergo a series of evaluations for each of the five feasibility studies at intake, one month (just before discharge), and three months later. Core staff will carry out the interviews and coordinate the follow-up, helping to facilitate testing to be carried out by personnel on the five feasibility studies.

RESEARCH PROJECT #2: **LESS INTENSE REACTION TO BRAIN DEPRESSANTS IN SONS OF ALCOHOLICS**

PROJECT DATES: 03/1/86 -- 02/28/89

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The proposed work is based on the premise that:

1) Alcoholism is genetically influenced;

2) Studying children of alcoholics might help identify potential markers of a predisposition towards alcoholism; and

3) Data demonstrating that sons of alcoholics (FHPs) show a decreased intensity of reaction to ethanol when compared to sons of nonalcoholics.

Our immediate goals are to further characterize these potential psychological/cognitive contributors to this phenomenon, and to home in on possible physiological/biochemical mechanisms contributing to the decreased intensity of reaction to FHPs.

We propose to begin to accomplish these tasks by using our research approach to determine the generalizability of the decreased reaction to ethanol to the level of reaction to another CNS depressant--diazepam. In this proposal, healthy, drinking, and nonalcoholic sons of alcoholics age 21 to 25 will be matched with sons of nonalcoholics on demography, drinking, and drug use histories, and height to weight ratio. Selected individuals will then be brought to the laboratory on four occasions where they will be challenged in turn with 0.7 ml/kg of ethanol, plus placebo diazepam; 0.1 mg/kg of diazepam, plus placebo ethanol; 0.2 mg/kg of diazepam plus ethanol, and placebo ethanol, plus placebo diazepam and their reactions observed over the subsequent four hours. The intensity of reaction to the challenge drug will be monitored through subjective and observer ratings of levels of intoxication, cognitive/psychomotor measures before and after the drug challenge, and hormonal responses during the laboratory session.

Co-Principal Investor

CINDY L. EHLERS, Ph.D.

RESEARCH PROJECT: #3 EEG MARKERS OF ALCOHOL INTOXICATION IN HIGH AND LOW RISK SUBJECTS

PROJECT DATES: 12/01/85 - 11/30/87

FINANCIAL SUPPORT:

DESCRIPTION OF PROJECT:

This study compares the drinking of non-alcoholic men age 21 to 25 years who have an alcohol first degree relative history negative for alcoholism. The project will measure all relevant aspects of the background cortical EEG on three separate occasions before drinking and after imbibing placebo. The baseline and post-drinking EEG patterns will be compared in the matched pairs to determine if these patterns are significantly different and might be trait markers associated with a vulnerability towards alcoholism.

A second objective is to use careful techniques to clarify some of the debate over the acute effects of alcohol on background cortical EEG's in healthy individuals (regardless of their family history). This will be facilitated by observing the effects over the three test sessions which include a placebo control and two active alcohol doses.

These objectives have led us to formulate the following proposed specific aims: 1) To identify a group of subjects, free of medical and psychiatric disorders, who have a family history (in first-degree relatives) of alcoholism, as well as a carefully matched control group; 2) To fully characterize the frequency, amplitude and time course of EEG spectra following low "intoxicating" doses of ethanol in human subjects regardless of family history; 3) To detect whether subjects with an alcoholic first-degree relative who are at elevated risk for alcoholism themselves, display quantitatible differences in EEG activity from control prior to or following administration of low doses of ethanol; 4) To explore possible correlations between EEG activity prior to and following ethanol administration and measures of past drinking history and present subjective and objective measures of intoxication.

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RESEARCH PROJECT: NEURONAL AND SYNAPTIC ACTIONS OF ALCOHOL
PROJECT DATES: 12/01/85 - 11/30/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism (NIAAA)

DESCRIPTION OF PROJECT:

The objectives of this component of the Alcohol Research Center is to determine the neuronal and synaptic sites most sensitive to acute or chronic intoxicating levels of ethanol, in an effort to pinpoint cellular loci responsible for behavioral intoxication. In addition, we will use electrophysiological methods to detect early excitatory neuronal activity concomitant with initial alcohol exposure that might underlie anxiolytic, euphorigenic or reinforcing actions of alcohol that could lead to alcohol addiction. Toward these aims we will employ a multi-model approach, in which the effects of ethanol and Tetrahydroisoquinolines (TIQ) on several key central nervous system target areas will be investigated with single unit techniques in vivo and in vitro. This multi-model approach will provide more detailed answers to questions of mechanisms of ethanol and TIQ action, and will serve to minimize artifacts of methodology. True postsynaptic ethanol effects will be proved by blockade of synaptic release with superfusion of 10mM $MgCl_2$. The possible effects of ethanol on voltage-dependent conductances will be studied with ion-specific toxins and ionic channel probes and by single and double electrode voltage-clamp methods. The effects of ethanol on intracellular free Ca will be further monitored in cultured neurons by the Arsenazo III method. The effects of temperature on responses to ethanol will be studied in the in vitro systems, with a view toward possible phase transition effects. In addition, most of these studies performed on brain areas of normal animals will be repeated on the same areas of animals treated chronically with ethanol, or withdrawn from such treatment.

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RESEARCH PROJECT #1: SAN FRANCISCO GENERAL HOSPITAL EMERGENCY ROOM STUDY
PROJECT DATES: 12/1/82 -- Ongoing
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The association of alcohol use to emergency room admissions is being analyzed using an interviewer-administered questionnaire and a breath test to estimate blood alcohol level on a 20 percent (20%) probability sample of all patients registering in the emergency room at San Francisco General Hospital during a 60-day period (December 9, 1984--February 6, 1985).

Data collected will be analyzed in relation to demographic characteristics, the injury or illness which brought the patients to the emergency room, the role alcohol played in the injury or illness, general drinking patterns of the patient, symptomatic drinking and whether the patient has received prior treatment for alcohol-related problems.

RESEARCH PROJECT #2: CONTRA COSTA COUNTY EMERGENCY ROOM STUDY
PROJECT DATES: 12/1/82 -- Ongoing
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

Same as San Francisco Study (#1 above) with a sample of 3,610 patients (a 50% probability sample), interviewed and breathalyzed in four hospital emergency rooms in Contra Costa County. Data were collected from April, 1985, to September, 1985, with three months of data collection in each emergency room.

RESEARCH PROJECT #3: CONTRA COSTA COUNTY HOSPITAL EMERGENCY ROOM CASUALTY STUDY

PROJECT DATES: 12/1/85 -- 11/30/90

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

One year of data collection (January 1987 -- December 1987) on a one-third probability sample of casualty patients at County Hospital in Contra Costa County. Study design, as in project #1 above. Also will be collecting data at the county coroner's office on those who do not make it to the emergency room.

Co-principal Investigator

DR. JUAN RODES
Barcelona, Spain.

RESEARCH PROJECT #4: ALCOHOL CONSUMPTION, INJURIES, AND MEDICAL PROBLEMS: A STUDY OF EMERGENCY ROOM STUDIES
PROJECT DATES: 7/86 -- 6/88
FINANCIAL SUPPORT: U.S.--Spain Joint Committee for Scientific and Technological Cooperation

DESCRIPTION OF PROJECT:

Similar to emergency room studies above, but design will allow cross-national comparisons of Bay Area emergency room data with data collected in Barcelona, Spain.

RESEARCH PROJECT #5: ALCOHOL CONSUMPTION, SOCIAL SUPPORT, AND INFANT OUTCOMES
PROJECT DATES: 5/86 -- 5/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism--Smithers Health Promotion Foundation, Inc.

DESCRIPTION OF PROJECT:

This project will collect and analyze data on the interaction of alcohol consumption and social support on pregnancy and infant outcome on 428 prenatal patients interviewed at public clinics located in a standard metropolitan statistical area between August, 1982, and June 1983.

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Co-principal Investigator

MICHAEL GEBERS, M.A.

RESEARCH PROJECT: DUI OFFENDER TRACKING SYSTEM (DOTS) STUDY
PROJECT DATES: 06/85 -- 05/87
FINANCIAL SUPPORT: Office of Traffic Safety

DESCRIPTION OF PROJECT:

This project involves the development of a computerized system for tracking accident and DUI recidivism rates of DUI offenders and tabulation of these rates by offender characteristics, geographical area, DUI sanctions, and type of program and identification of programs and sanctions that are maximally effective. This information will be summarized in MIS reports produced annually after the grant.

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Co-principal Investigator

RONALD STALL, Ph.D.

RESEARCH PROJECT: **ALCOHOL USE AND AGING: A 20 YEAR FOLLOW-UP STUDY**

PROJECT DATES: 02/1/86 -- 01/31/88

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

This project is intended to contribute to the understanding of how alcohol use and alcohol problems are related to disease, alcohol-related problems, decreased functioning, and mortality among the elderly by:

1) Explicitly focusing on changes in patterns of alcohol intake and alcohol problems over the life cycle;

2) Providing estimates of rates of alcohol-related morbidity and mortality which occur within community-based samples over a long-term follow-up period; and

3) Exploring how the functional abilities of the elderly are affected by prior levels of alcohol use.

The proposed study makes use of two samples of the San Francisco adult population. The first of these (n=970) was interviewed in 1964 and is representative of the adult population age 23 and over in San Francisco at that time. The second sample (n=786) was interviewed in 1967 and is representative of white males living in San Francisco aged 23-59 in that year.

We expect the proposed analyses will hold strong implications for both theoretical and practical concerns relevant to alcohol use and the aging process. The research will describe not only current levels of alcohol and alcohol problems among elderly persons, but also evidence on whether such problems are associated with earlier behaviors, beliefs, or psychological traits. It will allow the comparison of older drinkers who begin drinking in later life to those ex-problem drinkers who managed to resolve their problems, and to those drinkers who never had problems with drinking. This sort of comparison will contribute to the growth of a body of knowledge holding immediate health policy, prevention, and treatment implications.

WYLIE W. VALE, Ph.D.
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Co-Principal Investigators

J. RIVIER, Ph.D.
C. RIVIER, Ph.D.
P. PLOTSKY, Ph.D.

RESEARCH PROJECT: **NEUROENDROCRINE EFFECTS OF ALCOHOL**
PROJECT DATES: 12/01/85 - 11/30/87
FINANCIAL SUPPORT: National Institute of Alcohol Abuse and Alcoholism (NIAAA)

DESCRIPTION OF PROJECT:

Investigations in the Peptide Biology Laboratory are directed toward the characterization of the physiological roles, pharmacologic actions and chemical structure of regulatory peptides, which modify endocrine and brain functions. Furthermore, we are involved in the development of analogs of known peptides which might have therapeutic and/or investigational applications.

We are studying the effects of ethanol and its possible methabolites on various parameters of endocrine and central nervous system functions, and will explore the possibility that modulations in regulatory peptide regulation, metabolism or actions might mediate some of the acute intoxicating or longer term toxic pathophysiologic actions of ethanol. We are focusing on three neuroendocrine regulated systems which are influenced by ethanol exposure: The hypothalamic, pituitary gonadal axis; the hypothalamic pituitary adrenal cortical axis; the neural pathways regulating sympathetic nervous system.

There is little doubt that pathologic alterations in human gonadal and adrenal cortical functions are often associated with chronic alcoholism. Similar ethanol mediated changes are reported in experimental animals. In our studies, it appears that ethanol induced inhibition of gonadal functions may depend on factors which have not been clearly defined. We will explore the possibility that stress is such a factor. A major thrust of our proposal will be directed toward elucidating the role played by nonspecific stress in some of the acute and chronic neuroendocrine changes in ethanol-treated animals.

A series of experiments are planned to: 1) establish, confirm or extend information on the acute and/or chronic effects of ethanol on the three systems (gonadal, adrenal cortex, sympathetic nervous system; 2) study the initial site of ethanol's action on these systems with particular emphasis on the hypothalamic peptide components; 3) investigate the possible interaction of factors such as stress in the ethanol effects; 4) probe the roles of stress modulating peptides in the effects of ethanol and stress.

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RESEARCH PROJECT: **SOME ASPECTS OF TREATMENT OF WOMEN ALCOHOLICS: ALL-WOMEN VERSUS MIXED-SEX AA MEETINGS**

PROJECT DATES: 09/84 -- 01/87

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism -- University of California, Berkeley

DESCRIPTION OF PROJECT:

The aim of this research is to study women in Alcoholics Anonymous (AA) with a special focus on a comparison of their participation in all women's versus mixed meetings. The general questions of focus are:

1. What do they get out of each type of meeting?

2. Which do they prefer?

3. How do women in the different preference groups differ from each other in various social and psychological characteristics?

A qualitative design, in the tradition of Glaser and Stauss (1967) and in Schatzman and Strauss (1973) is the main approach for this study. Women who are at least 18 years of age, who have participated in the AA program for at least three years and have had at least three years of consistent sobriety are eligible for admission to the study. A researcher developed interview guide using primarily open-opened questions is the major tool for the study. The BEM (Bem, 1981) sex-role inventory will also be administered for the purpose of criterion or concurrent validity.

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RESEARCH PROJECT: **ALCOHOL RELATED TRAFFIC CRASHES**
PROJECT DATES: 04/1/84 -- 11/30/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

An assessment of the effect of increases in minimum purchase age on crash involvement and an examination of the effect of macro-economic changes on alcohol consumption and crash involvement. This research applies Box-Jenkins time series analysis to existing data sets to address previous topics.

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RESEARCH PROJECT: **ALCOHOL PROBLEMS AND PATHWAYS TO TREATMENT**
PROJECT DATES: 12/1/86 -- 11/30/87
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The Community Epidemiology Laboratory involves several studies focused on understanding the prevalence and types of alcohol problems and the community response system in one Northern California county. These include:

- A general population survey (1979);
- A survey of clients in the alcohol treatment system (1984-85);
- A survey of patients in hospital emergency wards (1985-86); and
- A survey of clients within the mental health system of the county (is currently under way).

In 1987 a general population survey and studies within the criminal justice and drug treatment systems will be conducted. During 1988-89 the social welfare system, family counseling agencies, and primary health centers will be surveyed. Each study will look at the prevalence of alcohol problems, drinking patterns and attitudes within its system's caseload and examine the process by which its clients came to treatment. The role of a wide variety of family and institutional responses will be examined. Analysis will also take place across data sets to provide a comparison of alcohol use and problems for the different kinds of respondents in the various programs. The studies taken together will provide a comprehensive look at how alcohol problems are defined and sorted across different health and social services systems.

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Co-principal Investigator

OTTO VON LEIRER, Ph.D.

RESEARCH PROJECT: **PILOT PERFORMANCE AND ALCOHOL**
PROJECT DATES: 9/86 -- 8/89
FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

We intend to study the effects of alcohol ingestion on aircraft pilot performance. This study will become part of a large programmatic investigation of the effects of "recreational" drugs on pilot performance that includes both alcohol and marijuana abuse.

Virtually no programmatic research has studied the course of alcohol's effects on pilot performance. This is surprising considering the fact that over 700 people have died in alcohol-related air crashes between 1975 and 1981 (10.1 percent of all crashes). While performance research shows significant cognitive and behavioral impairments related to the use of alcohol, the interaction of factors such as level of dose, the duration of drug effects, and task difficulty have not been studied with respect to pilot performance. Furthermore, these variables have not been examined in relation to such factors as alcohol usage patterns, level of fatigue, pilot's flying experience, and age of pilot. We plan to investigate these factors and their interactions in a series of four experiments.

The independent and dependent variables studies in these experiments were selected on the basis of existing findings and their ecological validity. The dependent measures are collected on relevant flight performance measures. All four experiments share a subset of four independent variables:

a) drug type;
b) alcohol dose level;
c) task difficulty; and
d) delay period between alcohol dose and test.

Experiment I asks what effects these four variables plus the pilot's level of recreational use of the drug have on performance.

Experiment II asks what effects these four variables plus pilot fatigue have on performance.

Experiment III asks what effects these four variables plus flying experience have on performance.

Experiment IV asks what effects these four variables plus age of pilot have on performance.

JEROME A. YESAVAGE, M.D.--PILOT PERFORMANCE AND ALCOHOL (Continued)

In these experiments we will be particulary concerned with the possible interaction effects of two or more variables.

The four experiments will be conducted over a three-year period using a flight simulator specifically developed for empirical research on pilot performance. Through these experiments we intend to obtain basic knowledge about the effects of alcohol on pilot performance.

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RESEARCH PROJECT: **HUMAN ALCOHOL DEHYDROGENASE AND ALDEHYDE DEHYDROGENASE**

PROJECT DATES: 04/01/86 -- 03/31/89

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

Utilizing the cDNA probes for human ADHs and ALDHs we cloned, the following studies will be undertaken:

1. Study of the genomic organization of three major ADH (i.e., ADH_1, ADH_2, and ADH_3) loci;

2. Study of the genomic structures of $ALDH_1$ (for cytosolic isozyme) and $ALDH_2$ (for mito-chondrial isozyme) loci;

3. Study of genotype distributions of the usual and atypical ADH_2 and $ALDH_2$ in Caucasians, Orientals, and American Indians, and in alcohol-sensitive and alcoholic subjects.

ALCOHOL AND DRUG

CHRISTINE BITONTI
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RESEARCH PROJECT: WOMEN IN TRANSITION PREVENTION EVALUATION
PROJECT DATES: 03/01/86 -- 12/31/88
FINANCIAL SUPPORT: California Department of Alcohol and Drug Programs

DESCRIPTION OF PROJECT:

Project Opportunity is a prevention programming effort linked to current theoretical developments in the field of stress and stress management. The theory that increased coping ability will lead to decreased use of substances during critical periods of life transition underlies the activities of the program during the three years of program operation. It is estimated that 250 to 300 women will participate in the program.

A followup evaluation of program participants is being conduced. A variety of data, with an emphasis on program activities, is being collected. The data collected during the program participation period includes pre- and post-tests on measures of esteem. Followup data on the participants' well being, aspects of their lives, and the effect of program services will be obtained via survey after the woman leaves the program. In addition, indepth interviews will be conducted for a selected sample of participants.

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Co-principal Investigator

DR. JOSEPH A. NOVACK

RESEARCH PROJECT: IMPAIRED SMALL TOWN PHYSICIANS AND THEIR SPOUSES

PROJECT DATES: 04/85 -- 12/86

FINANCIAL SUPPORT: California State University Faculty Development Program

DESCRIPTION OF PROJECT:

In spring, 1985, all spouses of physicians in Stanislaus County were sent a self-administered questionnaire. Approximately one-fourth of the questionnaires were returned. These replies will be used as a pilot study for a larger, longitudinal study of physicians and their families in California's Central Valley. The study concentrates on identifying those family-related factors that influence a physician's use of alcohol and prescription drugs.

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Co-principal Investigator

SUSAN G. MILLSTEIN, Ph.D.

RESEARCH PROJECT: **RISK TAKING BEHAVIORS IN ADOLESCENTS**
PROJECT DATES: Not stated
FINANCIAL SUPPORT: William T. Grant Foundation

DESCRIPTION OF PROJECT:

The behaviors associated with the major health problems of adolescents share a common theme--Risk-taking. Young people engage in potentially destructive behaviors with or without understanding the immediate and/or long-term consequences of their actions. Health education and prevention programs for youth have had minimal impact on reducing the mortality and morbidity secondary to risk-taking behaviors. Despite a general assumption among health professionals that certain behaviors are dangerous, with well-defined negative outcomes, little attention has been directed at trying to understand how adolescents conceptualize risk taking and its consequences. A better understanding of how adolescents perceive risk and the factors associated with those perceptions will enable us to develop intervention programs targeted at those perceptions and the associated behaviors. This proposal outlines a cross-sectional prospective study aimed at examining adolescents' concepts of risk and risk-taking behavior at certain critical points of physiological and psychosocial development. The proposal addresses three crucial problems areas in the adolescent population: substance use, accidents, and sexual behavior.

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RESEARCH PROJECT: **DEVELOPMENTAL ISSUES IN ALCOHOL AND DRUG DEPENDENCY**

PROJECT DATES: 06/84 -- 06/90

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism, and Private Funds

DESCRIPTION OF PROJECT:

This study utilizes a Black twin study model to examine the developmental precursors to alcoholism and substance abuse. The purpose of the research is to examine the formation and development of substance abuse in the Black family.

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RESEARCH PROJECT: ALCOHOL AND DRUG USE CONSUMPTION PATTERNS AND AIDS

PROJECT DATES: 02/86 -- 11/86

FINANCIAL SUPPORT: National Institute on Alcohol Abuse and Alcoholism

DESCRIPTION OF PROJECT:

The research project utilizes three existent data sets to determine the relationship between patterns of alcohol and drug consumption and the spread or development of AIDS. Two primary questions are being explored:

1) Is there an association between alcohol or drug consumption and participation in sexual activity likely to spread HIV infection?

2) Is there an association between level of alcohol or drug consumption and the degree of immune suppression among HIV antibody positive men?

The two primary research questions were chosen for their immediate implications for improving the efficacy of AIDS prevention efforts--at present the only available means of controlling this epidemic. If it can be shown that specific alcohol or drug use consumption patterns are implicated in high risk sexual behavior for the spread of HIV infection, then the efficacy of AIDS prevention efforts can be improved. Further, if it can be shown that specific levels of drug and/or alcohol use help trigger the manifestation of clinical AIDS, then prevention efforts can be designed which attempt to prevent the onset of AIDS among the growing number of antibody-positive individuals.

DRUGS

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RESEARCH PROJECT #1: THE NATURAL HISTORY OF NARCOTIC ADDICTION: A 25-YEAR FOLLOW UP
PROJECT DATES: 09/1/86 -- 08/31/87
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

Data collection in 1985-86 on the natural history of heroin addiction from 581, 1962-64 admissions to the California Civil Addict Program (CAP) will be analyzed. Archived data from a 1974-75 follow up interview of the same respondents will be integrated into the data base in order to provide a complete chronological history of each subject's addition career from 12 months prior to the first narcotics use to the time of interview--a period spanning over 25 years. Selected statistical techniques will be applied to the data to describe:

1) death rates and causes of death;
2) incarceration and legal supervision history;
3) narcotics use patterns and associated behaviors; and
4) treatment episodes and outcomes.

Multivariate analysis will be used to relate background and pretreatment variables to response to treatment and status at interview. Maturing out processes will also be examined and survival curve analysis applied to the attenuation of intervention effects. Other techniques applied to the data will include: time-series analyses, log linear modeling and distribution-independent simultaneous linear equation modeling.

Co-principal Investigator

YIH-ING HSER, Ph.D.

RESEARCH PROJECT #2: **ADDICT CAREER HISTORIES: PROCESSES AND PATTERNS**

PROJECT DATES: 07/1/86 -- 06/30/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This study is the continuation of the secondary analyses of 1,781 addict career histories (1,441 men and 337 women) accumulated from four long term follow up studies of chronic addicts identified from admissions to the California Civil Addict Program and various Southern California methadone maintenance treatment programs. The comprehensive data base includes demographics, family characteristics, and complete drug histories. Retrospective longitudinal interviews covering a period from 12 months prior to first narcotic use to interview provide behavioral data about narcotics use, legal supervision status, criminal behaviors and income, drug trafficking, employment marital status, and treatment episodes. Corroborative data were obtained from official records of arrest and methadone maintenance treatment for each subject and from a voluntarily provided urine specimen taken at interview.

Important answers to questions concerning opiate drug treatment issues and concerning criminal and social correlates of long-term opiate drug use will be obtained from the various data bases. These questions include:

1) How do Chicana women and Chicano men differ in their opiate use histories?

2) How do they differ in their opiate use etiology and their response to treatment?

3) How do addict subtypes differ in their propensity to finance their heroin addiction through property crime?

4) Will multivariate linear analyses replicate recent findings on maturing out obtained from log-linear analyses?

5) What are the social and demographic correlates of mortality in heroin addicts?

Sophisticated statistical methods will be applied to the analysis of the data. These include survival analysis, linear structural equation models for non-normally distributed data and multidimensional unfolding.

Co-principal Investigator

GEORGE R. SPECKART, Ph.D.

RESEARCH PROJECT #3: OPTIMIZATION OF LEGAL SUPERVISION FOR CHRONIC ADDICT OFFENDERS

PROJECT DATES: 09/1/86 -- 08/31/87

FINANCIAL SUPPORT: National Institute on Justice

DESCRIPTION OF PROJECT:

Research on crime control theory and the deterrence effects of criminal sanctions has produced results which have not been cause for optimism among social policy makers. The present research reviews and extends research which shows positive, demonstrable effects in the suppression of crime as a result of intensive, parole/probation supervision with urine monitoring among addictive drug users. The project extends this line of research into more detailed analyses by identifying optimal forms and levels of legal supervision as a function of previously determined addict typologies or categories. Data is presently available on 1,781 addict career histories which permits an exact specification of legal supervision effects within diverse addict types or subgroups in terms of changes in criminality, drug use and employment. The effects of legal supervision in the context of concomitant drug treatment programs are also demonstrable with this data. The benefits of the proposed research include:

1) The theoretical clarification of important issues of significant policy concern to the criminal justice system;

2) Empirically-derived guidelines for determining which probationers and parolees should be monitored for addictive drug use most strictly; and

3) Scientific evidence providing a foundation for legislative reform of urine monitoring procedures imposed on such individuals to improve the efficacy of supervision and crime control.

Co-principal Investigator

CINDY HIGASHI WADE
LAWRENCE M. SCHEIER

RESEARCH PROJECT #4: **CALIFORNIA DRUG ABUSE INFORMATION AND MONITORING PROJECT (DAIMP)**

PROJECT DATES: Ongoing

FINANCIAL SUPPORT: California Department of Alcohol and Drug Programs

DESCRIPTION OF PROJECT:

A major DAIMP project will be to monitor drug abuse trends throughout California with the assistance of an on-line computer networking system. This method of data collection will allow information to be analyzed and disseminated more rapidly than has been done in the past. Another project is a resource manual on drug abuse and pregnancy that is directed towards drug treatment programs and drug treatment providers (e.g., counselors and others who work with drug abusers). The manual will include materials on topics such as the identification of drug abuse in pregnant women, the factors which affect risk levels, information about the effects of specific drugs, the ethical and legal responsibilities of the health care provider, treatment approaches, the risk of pediatric AIDS, and the resources available to serve this particular population. Another aspect of the project includes a field ethnographer/epidemiologist who will monitor drug abuse in the community by conducting field interviews with relevant professional staff and members of the drug-using population.

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RESEARCH PROJECT: STRESS REACTIVITY: FAMILIAL ANTECEDENTS OF ADOLESCENT ADJUSTMENT

PROJECT DATES: 10/1/85 -- 09/30/87

FINANCIAL SUPPORT: W.T. Grant Foundation

DESCRIPTION OF PROJECT:

General objectives are:

1) Identify origins in family socialization practices of developmental competencies at four crucial developmental stages -- 4-5, 9-10, 14-15, and early adulthood; and

2) Provide an empirical basis for prevention and intervention in serious adolescent maladjustment including drug abuse, supportive of efforts of emerging concerned parent groups.

Specific aims are to test hypotheses that:

1) Stress-avoidant early parenting (Permissive) will produce low stress tolerance, regressive behavior, and low social assertiveness at adolescence;

2) Stressful early parenting (Authoritarian, Rejecting) will produce low self-esteem and delinquency in "vulnerable" children but social assertiveness in "hardy" children; and

3) Stress-monitoring early parenting (Authoritative) will produce well-adjusted, competent children who cope well with stress.

Additional aims related to adolescent drug use are to:

1) Establish personal and socialization antecedents and consequences of adolescent drug use and abuse;

2) Construct drug use categories for the purpose of establishing "breaking points" where functional decrement (e.g., amotivational syndrome) occurs.

Families (130-160 depending upon the specific panel analysis) are drawn from middle-class Caucasian residents of the San Francisco/East Bay area. At each time period, independent assessments are made by psychologists of the children and their parents using intensive clinical and social issues interviews, naturalistic and structured observations of family interaction in the home and laboratory and of the child at school, self-report data, and psychometric tests. A distinction is made between stressors and stress, and between eustress and distress, with the position taken that

DIANA BAUMRIND, Ph.D. -- STRESS REACTIVITY: FAMILIAL ANTECEDENTS OF ADOLESCENT ADJUSTMENT (Continued)

stressful crises offer growth-enhanced as well as growth-retarding opportunities. Theoretically guided hierarchical multiple regression and prediction analysis methods are used to compare child types on hypothesized antecedents and correlates, and to determine whether those aspects of parenting behaviors and child behaviors which are hypothesized to be associated with functional decrement resulting from drug use are in fact causally related to one another over time periods.

Co-principal Investigators

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RESEARCH PROJECT: **INTERGENERATIONAL FAMILY THERAPY WITH DRUG ABUSERS**

PROJECT DATES: 06/1/84 -- 05/31/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This project studies the impact of an intergenerational family therapy (IFT) program with heroin abusers and their families. The specific aims are to:

1) Assess the effects of ten IFT sessions on:

   a. Patients;
   b. Other family members (siblings and parents); and
   c. The family system.

2) Assess ethnic differences between Hispanic and non-Hispanic families of heroin abusers enrolled in methadone maintenance as shown by:

   a. Recruitment rates;
   b. Attrition from treatment; and
   c. Outcome measures.

Sixty adult heroin addicts (30 Hispanics and 30 non-Hispanics) from a methadone program and their families of origin will be assigned randomly to a family treatment or an attentional control condition consisting of didactic sessions on family life and the principles of family therapy. Measures occur at pre-, post-, and six-month follow up. The effects of treatment will be evaluated on:

1) Functioning of the patient (i.e., drug use, psychiatric symptomatology, treatment progress, social networks, and satisfaction with treatment);

2) Functioning of siblings and parents (i.e., levels of depression and anxiety, drug and alcohol use, attitudes and knowledge about drug abuse/addiction, and social networks); and

3) Functioning of the family system (family functioning, the family environment, and levels of cohesion and adaptability).

GUILLERMO BERNAL, Ph.D. -- INTEGENERATIONAL FAMILY THERAPY WITH DRUG ABUSERS (Continued)

The proposed research is a culmination of a series of clinical case studies and work with the families of heroin addicts conducted by the Principal Investigator. The study builds on the family therapy and research literature and will serve as a base to develop further research on the effects of different family therapy modalities on the treatment of substance abusers.

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RESEARCH PROJECT: COMMUNITY DRUG IDENTIFICATION SERVICE
PROJECT DATES: 09/19/70 -- Present/Ongoing
FINANCIAL SUPPORT: School of Pharmacy

DESCRIPTION OF PROJECT:

The identification of both "street drugs" and other unknown dosage forms.

Co-principal Investigators

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ANTHONY J. TREVOR, Ph.D.
THOMAS P. SINGER, Ph.D.

RESEARCH PROJECT #1: **BIOACTIVATION OF TERT-ALLYLAMINES (MPTP) TO NEUROTOXIND**
PROJECT DATES: 02/01/86 -- 01/31/87
FINANCIAL SUPPORT: National Institute of Neurological and Communicative Disorders and Stroke

DESCRIPTION OF PROJECT:

Studies are being pursued to characterize the bioactivation pathway of the nigrostriatial toxin MPTP--a compound which has caused Parkinson's disease in drug abusers who have been exposed to MPTP-contaminated street drugs. Mechanistic questions relating to the interactions of the MAO B generated reactive metabolities with key generating biological processes are being pursued. The MAO B substrate properties and neurotoxic potential of synthetic analogs are being assessed to identify the structural requirements for neurotoxicity.

Co-principal Investigators

ANTHONY J. TREVOR, Ph.D.

RESEARCH PROJECT #2: **IMINIUM METABOLITES FROM TERTIARY AMINES (PHENCYCLIDINE)**
PROJECT DATES: 07/01/86 -- 06/30/87
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

Studies are directed to the characterization of the metabolic fate of the psychomimetic agent phencyclidine with particular focus being given to the generation of chemically reactive metabolites which may contribute to the pharmacological and toxicological profile of this drug.

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RESEARCH PROJECT #1: CHEMICAL PHARMACOLOGY OF MDA AND MDMA
PROJECT DATES: 07/01/86 -- 06/30/89
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This project examines the pharmacological relationship between MDA and MDMA and the mechanism of neurotoxicity induced by the two compounds. The role of cytochrome P450 dependent metabolism in the toxicity of the compounds will be studied. Neurochemical studies of the parent compounds and the major metabolite, alpha methyl dopamine with central monoaminergic neurons will also be conducted.

RESEARCH PROJECT #2: CHEMISTRY OF PHENCYCLIDINE METABOLISM
PROJECT DATES: 08/01/85 -- 07/31/89
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This project investigates the metabolism of heterocyclic nitrogen compounds in phencyclidine, its congeners and other drugs of abuse. Studies with phencyclidine congeners have shown differences in ring metabolism with ring size. Subsequent studies will determine the effects of substitution on the alpha carbon of the ring on metabolism. The relationship between metabolism of the ring and inhibition of some cytochrome P450 mediated reactions will also be determined.

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RESEARCH PROJECT: CANNABIS THERAPEUTIC PROGRAM
PROJECT DATES: 1980 -- 1988
FINANCIAL SUPPORT: State and Federal Funds

DESCRIPTION OF PROJECT:

Evaluation of THC and marijuana for treatment of intraocular pressure in open angle glaucoma patients and as an antiemetic for cancer patients receiving chemotherapy or radiation.

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Co-principal Investigators

ROBERT ANDREW MOORE, Ph.D.
SHARON K. SMITH, Ph.D.

RESEARCH PROJECT #1: SERUM MORPHINE RIA KIT
PROJECT DATES: 01/87 -- 12/87
FINANCIAL SUPPORT: Commercial

DESCRIPTION OF PROJECT:

The purpose of these studies conducted at Diagnostic Products Corporation (DPC) and DPC's European Research Institute is to develop and bring to market a radioimmunoassay kit for detection of morphine in serum.

Co-principal Investigators

ROBERT ANDREW MOORE, Ph.D.
SHARON K. SMITH, Ph.D.

RESEARCH PROJECT #2: COCAINE METABOLITE RIA KIT FOR DRUG ABUSE
PROJECT DATES: 01/87 -- 12/87
FINANCIAL SUPPORT: Commercial

DESCRIPTION OF PROJECT:

The purpose of the studies conducted at Diagnostic Products Corporation (DPC) and DPC's European Research Institute is to develop and bring to market a radioimmunoassay kit for detection of cocaine metabolite in urine.

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RESEARCH PROJECT: **PROJECT ALERT: A SMOKING AND DRUG PREVENTION EXPERIMENT**

PROJECT DATES: 06/15/83 -- 02/28/90

FINANCIAL SUPPORT: Conrad N. Hilton Foundation

DESCRIPTION OF PROJECT:

Project ALERT is an innovative, school-based drug prevention program for adolescents. Based on the social-influence model of initiation into drugs, it seeks to prevent both experimentation with drugs and transition to regular use by training young people to resist pressures to use these substances. Questions the experiment is designed to answer include:

1) How well does the social-influence approach work in preventing use of cigarettes, marijuana, alcohol, and other drugs?

2) How well does the model work across a variety of school environments?

3) Does the program prevent both experimental and regular use?

4) Is the program equally effective when delivered with and without the assistance of teen leader?

5) How long do program effects persist?

Beginning in the fall of 1984, Project ALERT was tested in seventh grade classrooms in 30 West Coast schools. The following year, students in the treatment schools received three booster sessions. Participating schools were randomly assigned to one of three groups. Two groups were taught the Project ALERT curriculum that helps motivate students not to use drugs and teach them how to identify and resist pro-drug pressures. Older teen leaders assisted the health educator in one of these groups; in the second group,, the health educator presented the curriculum without the help of teen leaders. A third group, the control, received no special curriculum.

To evaluate the program's preventive effectiveness, self-report and physiological data about drug and cigarette use were collected before the program began, at the end of the seventh grade sessions, and before and after the eighth grade sessions. Usage data will again be collected during the ninth and tenth grades. To measure how successfully the program has been implemented, Rand staff monitored classroom sessions and asked participating student, health educators, and teen leaders to complete short evaluation forms.

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RESEARCH PROJECT: NEURONAL SUBSTRATE OF OPIATE ANALGESIA
PROJECT DATES: 02/01/86 -- 01/31/89
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

There is a body of evidence implicating the neurons of the rostral ventral medulla (RVM) in modulation of pain and, particularly, in mediating the analgesic effects of systemically administered opiate drugs such as morphine. Endogenous opioid peptide-containing neurons and terminals are present not only within RVM but are also present in other CNS sites that project to and receive projections from the RVM. In addition to enkephalin, there is evidence the serotonin, noradrenalin and other putative neurotransmitters are present in nerve terminals in RVM.

Our goal is to elucidate the internal circuitry and function of RVM, particularly the role of opioid peptides. The strategy is to define RVM neuron cell classes on the basis of their receptive field and relationship of their discharge to nocifensive behavior. We will then map the location of each class and determine whether cells of the class project to the spinal cord. The effect on each class of either systemically injected or iontophoresed opiates or other putative neurotransmitters will then be studied.

In addition to better understanding of pain-modulating networks in the CNS, these studies, by defining the roles of both opioid and nonopioid neurons may suggest new classes of centrally-acting analgesic drugs.

Co-principal Investigators

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RESEARCH PROJECT #1: **TELEVISION SCHOOL AND FAMILY PROJECT (TVSP)**
PROJECT DATES: 1982 -- 1986
FINANCIAL SUPPORT: ALA, AHA, NCI, National Institute on Drug Abuse and KABC-TV and Feeling Fine Production Company

DESCRIPTION OF PROJECT:

The objective is to assess the relative efficacy of a combination classroom instruction and TV component program for smoking prevention with respect to students' smoking behavior and students' knowledge, attitudes, and beliefs about substance abuse.

In the Los Angeles areas, 50,000 seventh grade students received a cigarette smoking prevention classroom curriculum and media component utilizing social resistance training. The media component was produced by KABC evening news and aired in two parts in February, 1982. Five, five-minute segments on local KABC covered prevention, and five, five-minute segments covered cessation. Dr. Arthur Ulene narrated throughout. Students in the treatment condition were encouraged to view the programs with their parents. Students from matched schools provided a control comparison. A third group was identified as an encouragement-only condition. These students did not receive the classroom component but were encouraged to view the media program. Data were collected at baseline, immediately after the treatment, and at one and two years after the treatment.

Project results are under review for publication. They led to the development of a second-phase prevention/cessation project, i.e., Television School and Family Project (TVSFP)--see Project #2.

Co-principal Investigators

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RESEARCH PROJECT #2: **TELEVISION SCHOOL AND FAMILY PROJECT**
PROJECT DATES: 09/84 -- 08/89
FINANCIAL SUPPORT: National Institute on Drug Abuse and KABC-TV and Feeling Fine Production Company

DESCRIPTION OF PROJECT:

The objective or purpose is to determine the optimal combination of media and classroom instruction emphasizing social resistance training and family-oriented smoking prevention/cessation for seventh grade students and smoking parents. The programs were provided in February and March, 1986; the TV program aired on KABC-TV. The study consists of a 2 x 2 factorial design (TV-or-not by classroom-instruction-or-not) in Los Angeles (with controls oversampled to provide a test of an attention-placebo or expectancy control vs. a traditional control), supplemented by two cells (classroom only and control) in San Diego to control for possible media contamination. The study is being conducted as an efficacy trial to test the relative effectiveness of program components implemented under optimal conditions. Junior high school complexes were assigned randomly to experimental conditions from matched clusters. Approximately 1,000 seventh grade students were in each of the seven cells. Measurement of student/parent knowledge, attitudes, social normative beliefs, self-efficacy, smoking behavior, and intended behavior have been obtained at pretest and immediate posttest. One-year and two-year follow up data are to be collected.

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RESEARCH PROJECT: **CHEMICAL AVERSION THERAPY IN THE TREATMENT OF COCAINE DEPENDENCE AS PART OF AN OVERALL TREATMENT PROGRAM**

PROJECT DATES: 05/85 -- 12/86

FINANCIAL SUPPORT: Insurance and Investigator's donation of his time.

DESCRIPTION OF PROJECT:

Ten patients with primary cocaine dependence and 15 patients with primary alcohol and cocaine dependence entered into a treatment program. Chemical aversion therapy was used to develop an aversion to the sight, smell, taste, and thought of cocaine. These users were primarily snorters. An artificial cocaine was developed to provide a substance that was white, looked like cocaine, and had local anesthetic properties and a cocaine aroma was used to enhance the stimulus. Patients also then received group and individual counseling along with the aversion therapy.

Only one patient left the program against medical advice. Twenty-three of the remaining 24 patients were followed up on in six months with over 90 percent significant-other validation, 64 percent of the patients dependent on cocaine had been abstinent since treatment, and 64 percent of the patients dependent on alcohol and cocaine have been abstinent since treatment.

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RESEARCH PROJECT: **MONOAMINES AND HALLUCINOGEN'S EFFECTS ON RAT BEHAVIOR**

PROJECT DATES: 09/01/81 -- 05/31/88

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

In order to clarify the involvement of central noradrenergic systems and the nature of the alterations in behavioral responses to environmental stimuli produced acutely by hallucinogenic drugs, we propose to extend our studies of the effects of lysergic acid diethylamide (LSD), N,N-dimethyltryptamine (DMT), and 2,5-diemthoxy-4-methylamphetamine (DOM) to include more indoleamine and phenylethylamine hallucinogens, specifically, psilocybin, 2,5-dimethoxy-4-ethylamphetamine (DOET), and mescaline. The behavioral effects of these hallucinogens in male rats will be thoroughly characterized and compared using measures of tactile startle responses and a computerized Behavioral Pattern Monitor that provides detailed information regarding the amount and qualitative patterning of spontaneous activity and investigatory responses to specifiable familiar and novel stimuli in the environment. Rates of habituation of startle and exploration and the animal's sensitivity to novelty will be explicitly measured. The effects of selective neurotoxic lesions of specific noradrenergic pathways in brain will be similarly characterized. The effectiveness and specificity of each lesion will be quantified by both microspectrofluorimetric measures of formaldehyde-induced monoamine fluorescence and high-performance liquid chromatographic assays of regional monoamine levels using electrochemical detection. The possible mediation of the hallucinogen's effects by noradrenergic systems will be examined by testing the hallucinogens in lesioned animals and following pretreatments with selective antagonists or agonists, such as propranolol or clonidine. To minimize the confounding effects on the peripheral sympathetic nervous system, the adrenergic agonists and antagonists will be slowly infused into specific forebrain regions such as the hippocampus currently with the behavioral measures. The behavioral effects of these drugs will also be assessed to further delineate the influences of noradrenergic systems on activity, habituation, and responsiveness to exteroceptive stimuli.

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RESEARCH PROJECT: ENDOGENOUS OPIOIDS AND THEIR RECEPTORS
PROJECT DATES: 1975 -- Present
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This project continues work on the dynorphin opioid peptides and on the multiple opioid receptors. The dynorphins of various molecular weights from spinal cord and brain are being compared in order to find out about their role in pain regulation. Binding methods are being developed to distinguish the different types of opioid receptors in brain and other tissues. Actual morphine and codiene have been found in beef and rat brain, but it is not yet known if they are made there or enter through the diet, and in any case if they have a physiological role.

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RESEARCH PROJECT #1: **MARIJUANA SMOKING TYPOGRAPHY AID DOSE REGULATION**

PROJECT DATES: 05/01/84 -- 04/30/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

We will determine the extent and the means by which people regulate tetrahydrocannabinol (THC) and other substances absorbed during marijuana smoking. Comparisons between adolescent and adult marijuana smokers, frequent and infrequent users, males and females, those who also use tobacco, and nontobacco users will demonstrate the techniques, the limits, and the magnitude of dose regulation while smoking marijuana of various potency. Reliable measurement techniques already developed will be applied to the cannibis dosimetry research. Puffing and inhaling patterns, including puff volume measured by flow meter techniques, and inhalation volume measured by inductance pneumography, will provide a noninvasive and precise profile of how each cigarette is smoked on a puff-by-puff basis. Cardiovascular, autonomic, and subjective effects and plasma THC, 11-hydroxy THC, 11-nor-9-carboxy THC, and carboxyhemoglobin measures will allow determination of relationships between smoking patterns, resulting blood levels, and effects. Propranolol-induced beta adrenergic blockade and resulting changes in smoking behavior will examine the importance of autonomic system feedback in dose regulation.

The health significance of a smokers' dose control is only recently being appreciated by some researchers in tobacco studies. It may be of similar importance to marijuana smokers. Several disciplines, including psychopharmacology, psychophysiology, respiratory physiology, pharmacokinetics, and behavioral medicine, are involved. The studies have direct public health implications since, as with any drug, dose is likely to be related to both acute and long-term consequences. The relationships between marijuana potency and resulting amounts of material absorbed have been little studied. Only incomplete measures of smoking behavior have been previously used in marijuana research. The detailed examination of marijuana smoking behavior in adolescent smokers may enhance prevention strategies.

RESEARCH PROJECT #2: EFFECTS OF THE TOLERANCE--DEPENDENCE ON MARIJUANA SMOKING

PROJECT DATES: 04/01/84 -- 09/30/86

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

The relationship between the development of tolerance and physical dependence to tetrahydrocannabinol (THC) and marijuana self-administration by smoking will be determined. Changes in levels of drug self-administration have rarely been studied in situations where level of tolerance or abstinence is independently manipulated by the experimenter. Marijuana has characteristics that make it ideal to test determinants of drug self-administration that may be applicable to may drugs. The experiments should also provide useful new information specific to marijuana. Twenty experienced marijuana smokers living in a research ward for 25 days will be given repeated doses of oral THC at strengths to produce two levels of tolerance (10mg and 20mg doses). In previous experiments the higher dose level was reliably followed by an abstinence syndrome after eight days of intoxication. During periods of placebo and oral THC administration, subjects will be allowed free access to marijuana cigarettes with the amount smoked and physiologic and psychologic effects carefully measured. Measures of smoking behavior include puff volume and inhalation depth measures and repeated measures of cardiovascular, EEG, and symptom and behavior changes. Plasma THC and THC metabolite levels will be measured. Changes in marijuana smoking, dose absorbed, and effects will be followed through cycles of acquired tolerance and withdrawal over a 25-day period.

Methods involve disciplines of psychopharmacology, psychophysiology, pharmacokinetics, and behavioral medicine. Health implications include a better understanding of determinants and consequences of drug self-administration, and particularly marijuana administration.

RESEARCH PROJECT #3 — COCAINE PHARMACOKINETICS AND PHARMACODYNAMICS
PROJECT DATES: 08/01/81 -- 11/30/86
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

A long-term objective is to understand the pharmacology of cocaine. The pharmacokinetic characteristics and effects of cocaine and some of its major metabolites will be measured in human volunteer research subjects. Higher dose levels will be studied than has hereto been done in controlled laboratory studies. Bioavailability and other standard pharmacokinetic indices will be measured after intravenous, oral, nasal, and buccal routes of administration. Particular attention will be paid to investigation of kinetics and possible biological effects of benzoylecgonine and ecgonine methyl ester. Dose dependent kinetic differences will be explored after both single dose and intravenous infusions under steady state conditions. In vitro experiments will investigate mechanisms accounting for individual differences in metabolism and response. The possible effects of benzoylecgonine, such as they can be separated from the effects of cocaine, will be measured. Gas chromatographic assays of plasma and urine will measure cocaine, benzoylecgonine and ecgonine methyl ester levels. Heart rate, blood pressure, skin temperature, blood catecholamine levels and electroencephalographic evoked potential and spectral analysis measures will assess cocaine and metabolite effects. Subjective symptoms and mood will be measured. Better understanding of cocaine pharmacology and particularly benzoylecgonine and ecgonine methyl ester metabolism has significance for assessing the health consequences of cocaine use as well as resolving forensic toxicologic questions. Benzoylecgonine is being used as a marker of cocaine use and ecgonine methyl ester has been suggested as a useful marker, yet little controlled quantitative research, particularly relationships between cocaine dose and time of last use and metabolite levels, has been done in humans with those metabolites. The proposed studies should provide necessary information for further investigations of cocaine interactions with other drugs; for example, neuroleptics, antidepressants, nicotine, cannabis, opiates, other stimulants, and drugs that may help understand cocaine's mechanisms of action.

RESEARCH PROJECT #4 — DRUG DEPENDENCE CLINICAL RESEARCH PROGRAM
PROJECT DATES: 02/01/78 -- 12/31/87
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This multidisciplinary program project includes clinical and basic studies of factors influencing the development and loss of tolerance to and dependence on opiates,CNS depressants, cannabinoids, cocaine, tobacco, and opiate-like peptides and other drugs that may interact in clinical situations. The approach is a multidisciplinary one.

Specific studies include:

- Acute tolerance to and dependence on opiates and alcohol; and
- Clinical studies of the interaction between prior and current drug use and coexisting disease, particularly pharmacokinetic interactions.

Both human and animal studies will examine the metabolism and pharmacology of nicotine and nicotine metabolites, drug interactions between other drugs and nicotine so as to fully understand factors which influence tobacco smoking behavior responses. Basic studies of the biochemical basis of tolerance and dependence will continue with emphasis on hormones, cyclic nucleotides and calcium in their role as regulators and how they may interact with many drugs of abuse. Clinical trials of promising novel treatments of opiate dependence will emphasize the application of various nonnarcotic treatment approaches and the application of various psychosocial interventions as they may change drug-seeking behavior. The development of research strategies appropriate to the study of multiple drugs and interacting drugs rather than a narrow specialization in a particular substance or class of drugs is a guiding philosophy.

RESEARCH PROJECT #5 — NEUROPSYCHOPHARMACOLOGY OF ALTERED CONSCIOUSNESS

PROJECT DATES: 07/01/77 -- 06/30/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

My broadest objective is to:

1) Understand why people take psychoactive drugs;
2) What are expected effects;
3) What might account for unexpected effects; and
4) What it the role of tolerance and dependence in determining individual differences in drug use and effects.

Since I'm searching for common factors relevant to drugs of sometime quite different pharmacologic classes, I will continue to study a number of psychoactive drugs.

- The pharmacokinetics and dynamics of cocaine, when administered by smoking and by chewing, will be one part of a series of studies with that drug.

- The precise role of nicotine, and particularly nicotine titration in tobacco dependence, will be investigated in continuing laboratory and clinical treatment studies.

  - Precise quantitation of smoking behavior and concurrent measures of absorbed drug is one methodology.

  - Clinical treatment manipulations and long-term follow up of changes in smoking behavior is another method.

- Studies with cannabinoids will investigate relationships between tolerance and dependence and changes in marijuana smoking.

- When funded, studies of chronic cocaine administration in hospitalized volunteers will investigate some aspects of cocaine tolerance and dependence.

In all studies equal attention is given to psychological and behavioral data, subjective reports, and neurophysiologic and neurochemical data. The hope is that a better understanding of relationships between behavioral, physiologic and pharmacologic variables will result. A variety of biochemical, physiologic, neuroendocrinologic, behavioral, and psychometric techniques are used to assess effects and consequences of both acute and subchronic treatment. Research strategies appropriate to the study of different classes of drugs, rather than specialization in a particular method or a particular class of drug, will continue as a guiding philosophy. Where possible in human studies, mechanisms and explanations accounting for individual differences in consequences will be investigated. The studies are multidisciplinary, involve human subjects only, and should further understanding of human drug use.

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RESEARCH PROJECT: #1 **CENTRAL MECHANISMS OF OPIATE REINFORCEMENT**
PROJECT DATES: 02/02/86 - 01/31/89
FINANCIAL SUPPORT: National Institute on Drug Abuse (NIDA)

DESCRIPTION OF PROJECT:

Recent work in our laboratory has established the region of the nucleus accumbens as an important substrate for the reinforcing properties of heroin in non-physically dependent rats. Rats self-administering heroin intravenously show increases in self-administering after injection with systemic naloxone or central injection of the quarternary derivative of naloxone, methylnaloxonium. Direct intracerebral injections show that the region of the nucleus accumbens appears to be particularly sensitive to these injections. Also denervation of nucleus accumbens severely disrupts cocaine but not heroin self-administration. These results suggest an important role for opiate receptors in nucleus accumbens in opiate reinforcement and that these receptors are not localized on presynaptic DA terminals. The purpose of the present project is to continue these studies aimed at exploring the central mechanisms involved in opiate reinforcement and to extend these studies to exploring the central mechanisms involved in opiate dependence. Experiments are designed to examine further the role of the nucleus accumbens and its efferent projections in opiate reinforcement in nondependent animals, and to compare these results with similar studies in physically dependent animals. At the same time the neuronal sites of action important for opiate withdrawal will be explored in dependent animals by using local intracerebral injections of methylnaloxonium. Withdrawal measures will include unconditioned and conditioned behavior. Finally an attempt will be made to define the functional substrate for the phenomenon of conditioned narcotic withdrawal by attempting to reverse conditioned withdrawal with local intracerebral injection of morphine or opioid peptides. Results will have important implications for our understanding of the neural substrates involved in opiate seeking behavior and the addictive process.

RESEARCH PROJECT: #2 NEURONAL SUBSTRATES OF COCAINE REWARD
PROJECT DATES: 04/01/87 - 03/31/91
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This project investigates our understanding of the neuronal substrates for psychomotor stimulant reward and also important basic information about the organization of the neuronal substrates of reward in general.

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RESEARCH PROJECT: B-ENDORPHIN RECEPTOR: RELATIONSHIP TO MU AND DELTA BINDINGS

PROJECT DATES: 06/29/76 -- 06/30/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

We will continue our efforts to characterize receptor properties of endogenous opioids, and will study sequences not previously tested. We also will utilize ^{3}H-dynorphin to study this peptide's binding sites directly, and its interaction with other ligands. Overall, we will proceed as outlined in the present proposal.

Co-principal Investigators

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RESEARCH PROJECT: **STRUCTURAL-STRATEGIC FAMILY THERAPY WITH ADOLESCENT DRUG ABUSERS**

PROJECT DATES: 07/01/85 -- 06/30/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

The purpose of the study is to measure the relative effects of three forms of treatment for adolescent drug abuse: 1) family therapy, 2) group therapy, and 3) family education classes.

One hundred and fifty (150) adolescents will be randomly assigned into one of these conditions, and a sample of 50 nonclinical adolescents and their families will comprise a normative, comparison group. This group will be appropriately matched with the clinical sample on predetermined variables. The study's instrumentation includes self-report, perception of others, and observer-related family interaction tasks, as well as process level measures to assess between and within session mechanisms of change.

Five assessment points exist in the study: pre- and post-treatment, plus follow up measurement at 6, 12, and 24 months after the conclusion of treatment. The administration of each treatment condition is monitored through carefully controlled procedures. The providers in each of the conditions have received intensive training in their respective conditions and in adolescent drug abuse. Each provider receives weekly in-person supervision throughout the year. Four (4) well-established, high volume Bay Area youth and family serving agencies have agreed to serve as project sites. These agencies will provide the comprehensive services necessary for the completion of the project, e.g., the three treatment conditions, conduct of assessment sessions, etc. The project has also established its own clinical operation at SFGH and is receiving appropriate referrals at that site.

The overall goal of the project is the development of more cost-effective service models for the treatment and prevention of adolescent substance abuse. This second year of the study will focus on continuance of the treatment phase, further standardization of the training and treatment manuals for each condition, and production of other tangible results in the form of preliminary data analysis, and the editing of video training tapes for use by drug abuse professionals. One intended longer-range product is a practical manual of results for service providers and administrators which will help bridge the gap between research and treatment.

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RESEARCH PROJECT: NEUROCHEMICAL BASIS OF NARCOTIC ADDICTION
PROJECT DATES: 01/01/79 -- 12/31/90
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

The molecular mechanisms of opiate tolerance and dependence remain unknown, and efforts to elucidate them are greatly hampered by the complexity and heterogeneity of the brain. Our approach to this problem has been to use a clonal cell line of neuronal origin (NG108-15), initially described by Klee and Nirenberg (1975). These cells undergo a quantifiable biochemical response-inhibitation of adenylate cyclase when administered opiates and a tolerance-like adaptation process during chronic treatment.

We propose to study in detail the molecular mechanisms of the cellular adaptation processes and to determine their relevance to the mechanism of tolerance and dependence in mammalian brain. Specifically, we will:

1) Attempt to show that opiate receptor desensitization results from a covalent modification of the receptor, possibly dephosphorylation, allowing it to remain physically coupled to the regulatory subunit of adenylate cyclase (Ni), but unable to promote dissociation of GDP;

2) Show that during down-regulation, opiate receptors internalize in NG cells by a pathway similar to that traversed by other down-regulated receptors, and we will try to establish the exact nature of this pathway. We will also determine the kinetics of internalization and the signal initiating it;

3) Study the relationship of intracellular Ca++ to the up-regulation of adenylate cyclase activity by altering Ca++, by determining whether a cyclase-stimulatory material from up-regulated cells is calmodulin, and by investigating the role of polyphosphoinositide turnover in up-regulation;

4) Differentiate NG108-15 cells, and compare chronic opiate effects in them to undifferentiated cells; and

5) Investigate the recently discovered phenomenon of down-regulation in mammalian brain to determine which opiate agonists can initiate it, and whether receptors are internalized in the process.

Staff

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F. FATIMA MATOS

RESEARCH PROJECT: **PHARMACOLOGIC DEFINITION OF THE OPIOID RECEPTOR SELECTIVITY OF SELECTED AMINOTETRALIN ANALOGS**

PROJECT DATES: 11/04/82 -- 11/03/87 (final data not fixed)

FINANCIAL SUPPORT: University of the Pacific

DESCRIPTION OF PROJECT:

The goal of this research is to characterize the opioid receptor specificity of a series of aminotetralin analogs synthesized at the University of the Pacific by Dr. David S. Fires and associates. These compounds have been designed to have selective agonist and/or antagonist capacity. Interest has concentrated on two compounds with selectivity for mu receptors, one of which (3-dimethylamino-2,2-dimethyl-7-hydroxy-1-tetralone) is an agonist while the other (3-dimethylamino-2,2-dimethyl-7-hydroxy-1-tetralol) is a full antagonist. Test systems include the guinea pig ileum longitudinal muscle preparation of Kosterlitz et al (1970) and the mouse vas deferens preparation of Henderson et al (1972). Reference compounds include mu agonists (N-normorphine; dihydromorphine), delta agonists (leucine-enkephalin; D-alanine^2, D-leucine^5 enkephalin) and kappa agonists (ethylketocyclazocine; dynorphin 1-13) along with selected antagonists (naloxone).

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RESEARCH PROJECT: PREPARATION OF Δ^9THC AND LAAM
PROJECT DATES: Ongoing
FINANCIAL SUPPORT: Internal: Norac Company, Inc.

DESCRIPTION OF PROJECT:

Continuing research to improve the method of preparation of Δ^9THC and LAAM.

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RESEARCH PROJECT: **YOUTH SUBCULTURE VERSUS INDIVIDUAL FACTORS IN ADULT DRUG USE**

PROJECT DATES: 1984 -- 1986

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

In this study we interview a random sample of men and women who were members of two Los Angeles gangs. We compare those who were active in the 1940s with those active in the 1970s. Because our research staff includes former members of the gangs we have been able to compile rosters of original members and to locate a high proportion of those drawn in the sample.

The purpose is to analyze the relative influence of peer-group (i.e., gang) and family variables in later-life drug use and related problems of adjustment. Membership in these gangs represents a high risk for drug use in both adolescence and adulthood. In fact a high proportion of these respondents have used heroin. We obtain lifetime retrospective information on drug and alcohol use.

We focus on the following family variables:

- Composition and changes in composition throughout childhood and adolescence;
- Socio-economic status;
- Family interaction patterns;
- Ethnic factors;
- Family traumas and runaways.

We also analyze the timing of major life events, e.g., leaving school, drinking, having sex, getting married, and having children.

We focus on the following gang variables:

- Characteristics of the respondents' best friends in the clique;
- Motivations for belonging to the gang;
- The role of drugs and fighting;
- Other activities.

We include attitudinal questions relating to gender role, to drugs, and to the sense of integration in the larger society. Other "outcome" variables, in addition to drug use, include characteristics of the respondent's family of procreation, current and recent jobs, and experiences with imprisonment. We expect to find gender as well as "epoch" differences in variables associated with successful maturing out of gang-related drug use.

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RESEARCH PROJECT: NEUROTRANSMITTER RECEPTORS IN AGING MAMMALIAN BRAIN

PROJECT DATES: 6/83 -- 6/88

FINANCIAL SUPPORT: John Douglas French Foundation, National Institute on Aging

DESCRIPTION OF PROJECT:

We are continuing a second phase of our research concerning age-related changes in serotonin and dopamine receptors in the central nervous system. Our first phase involved developing the receptor assays for D-1, D-2, S-1 and S-2 receptors. We applied these techniques to "nonpathological" aging questions in post-mortem human brain and the aging C57BL/6J mouse model.

The second phase of this project considers receptor changes in neurodegenerative diseases with delayed onset such as Alzheimer's disease and Parkinsonism. These results will be interpreted in the context of the nonpathological age-related changes found previously.

A third, parallel phase of this project examines the effects of psychoactive drug administration on receptor dynamics as a function of age. Antidepressant and neuroleptic drugs will be administered to mice of several age groups, and receptor regulation by these compounds will be estimated to determine if receptor regulation is affected by aging.

In all projects, measurements of monoamine levels by HPLC and measurements of various enzyme activities will be correlated with receptor changes.

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RESEARCH PROJECT: **AIDS RISK REDUCTION FOR NEEDLE-USING DRUG USERS**

PROJECT DATES: 07/01/85 -- 10/1/86

FINANCIAL SUPPORT: National Institute on Drug Abuse
City and County of San Francisco

DESCRIPTION OF PROJECT:

The study includes four distinct foci:

1) An epidemiological study of HIV seroprevalence and risk factors among 300 in-treatment IV drug users and 101 out-of-treatment IV drug users;

2) A formal ethnography of IV drug users in the Tenderloin and Mission neighborhoods;

3) A demonstration/evaluation of a model AIDS risk reduction/health promotion program that targets IV drug users not in treatment; and

4) Immunological functioning of 401 IV drug users.

HENRY RAPOPORT, Ph.D.
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RESEARCH PROJECT: **BIOORGANIC CHEMISTRY OF THE OPIUM ALKALOIDS IN VITRO**
PROJECT DATES: 01/01/86 -- 12/31/86
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This research is directed to:

1) The biosynthesis of the opium alkaloid;
2) Modified opiate structures with enhanced agonist and antagonist activity; and
3) A practical total syntheses of thebaine and codeine.

The biosynthetic work will focus on the enzymic conversion of reticuline to salutaridine and the metabolic fate of morphine in the plant. The modified opiate structures will be derived from etorphine and be elaborated with conformationally rigid nitrogen substituents. The total synthesis will emphasize economy of steps and control of asymmetry.

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Co-principal Investigator

GORDON T. PRYOR. Ph.D.

RESEARCH PROJECT: NEUROTOXICITY OF MARIJUANA IN SUBHUMAN PRIMATE
PROJECT DATES: 01/01/85 -- 12/31/88
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

Because marijuana is such a widely used drug and there are suggestions that prolonged use causes irreversible alterations in the brain, it is important to determine more definitively if there are persistent effects of marijuana use. To study the potential neurotoxicity of marijuana, behavioral, and neurophysiological responses of 32 young male Rhesus monkeys chronically exposed to marijuana smoke (5 days per week) are being evaluated.

Chronic dosing consists of exposing the monkeys to smoke from placebo cigarettes or the smoke from marijuana cigarettes (2.54% Δ^9-THC) one or more times daily, five days each week. To accomplish the exposure a monkey is seated in an airtight chamber with his head protruding. A face mask is connected to the output of an ADL-II smoking machine that delivers a fixed volume (35 ml) of smoke at a fixed rate (1, 2, or 3 times per minute). When the smoke is presented, the chamber is put under negative pressure, forcing the monkey to inhale the smoke deeply and hold it for six seconds. Then the vacuum is released and the monkey is allowed to breathe fresh air freely between puffs. The nominal dose is established by the number of puffs delivered; blood levels of Δ^9-THC and carboxy-hemoglobin are measured periodically as indices of dose consumed and carbon monoxide levels in the inhaled smoke. Prior to dosing, the monkeys were trained to perform a cued-reaction-time task and 14 cortical and subcortical electrodes permanently implanted for recording event-related potentials associated with the behavioral task, visual- and auditory- evoked potential, and the electroencephalogram (both spontaneous and driven by visual and auditory stimuli). These various measures of neurobehavioral function are being monitored on a regular basis throughout the chronic dosing phase, which will continue for up to one year. Following chronic dosing, the same measures will be monitored for an additional year to assess possible persisting neurotoxicity.

MARSHA ROSENBAUM, Ph.D.
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Co-principal Investigator

SHEIGLA MURPHY

RESEARCH PROJECT: METHADONE TREATMENT: A STUDY OF COUNTY POLICY CHANGE

PROJECT DATES: 02/01/85 -- 01/31/89

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

During the past five years there has been an increasing push for federal, state, and local agencies to cut back--sometimes in part, often in total--funding for formerly supported drug programs. The largest of the publicly supported drug abuse programs has been methadone maintenance--a treatment initially heralded as the ultimate cure for heroin addiction. The majority of methadone maintenance patients have counted on public support to pay for their medication, for an open-ended period. Yet both public attitude and budgets have changed regarding methadone maintenance policy. The former has become skeptical, the latter smaller-resulting in numerous proposals and some action that would alter the current methadone maintenance system.

As of October 1, 1984, Alameda County (the fifth most populous in California, with a population of 1,145,117 as determined by the 1980 census) will no longer provide funding for individuals who have occupied county-funded methadone maintenance slots for a period of two years or longer. These individuals have the option of transferring to private, paying slots or being detoxified. Three methadone clinics are affected by this new policy, and 300 clients at the outset. This proposal is designed to complete a four year study of 150 of the individuals initially affected by Alameda County's change in policy. The proposed study will follow each of the 150 clients for two and a half years to describe and analyze the impact of the new policy. Using the depth interview and a standardized questionnaire, each client will be interviewed both before (s)he is forced to relinquish his/her subsidized slot and thereafter at six month intervals. A total of five follow-up interviews will be completed in addition to the initial interview. The interview will be designed to gather information in the following general areas of the client's life; means of financial support; means of securing drugs (including methadone); drug and alcohol use; physical health status; mental health status; social situation.

Completion of the proposed study will allow a unique opportunity to study, on an actual first-hand basis, the implications for a shift in drug treatment policy such as Alameda County's. If, as seem to be the trend, other counties and states are to move in this direction, it is imperative that consequences to clients' lives and public welfare be understood--as this project proposes.

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RESEARCH PROJECT: EFFECTS OF METHADONE ADDICTION ON RATS
PROJECT DATES: 1975 -- Present
FINANCIAL SUPPORT: Institution Funds, Claremont Colleges

DESCRIPTION OF PROJECT:

We have developed a model for methadone addiction in rats in which the animals show a compulsion, tolerance and withdrawal symptoms. The model is being used to study the effects of maternal addiction of offspring, using a rat model for neurobehavioral development. In addition, we are examining the effects of the drug on cyclic nucleotide levels in those areas of the brain involved in addiction. This is being done to test a model in which addiction is related to these nucleotides.

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RESEARCH PROJECT: **OPIOID RECEPTOR BINDING IN VIVO AND EFFECTS IN RATS AND NEUROBLASTOMA CELLS IN CULTURE**

PROJECT DATES: 09/30/84 -- 07/31/89

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

One portion of this proposal deals with the relationship among the pharmacokinetics, stereo-specific cerebral binding to receptor sites, and pharmacodynamic effects of opiate drugs. Specific hypotheses to be tested include the existence of multiple opiate receptor sites and the contribution of each receptor site to various opiate effects (e.g., mediating analgesia or addiction/withdrawal). Another portion of the project includes the molecular characterization of opioid receptors in neuroblastoma cell lines in culture. Specifically, human neuroblastoma cell lines expressing the opiate receptor are evaluated as cellular models of opiate tolerance and dependence.

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RESEARCH PROJECT #1: BEHAVIORAL PHARMACOLOGY OF OPIATE-LIKE NEUROPEPTIDES
PROJECT DATES: 07/01/78 -- 11/30/88
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

Converging evidence suggests that endogenous opioid systems (EOS) may play an important role in modulating behavioral responsiveness to stressful situations. However, further progress is limited, in part, because of inadequate or incomplete behavioral characterization of various opioid and stress treatments. In addition, comparison of these effects would be greatly facilitated if the behavioral characterization was carried out under similar experimental conditions. Our behavioral system has been specifically designed for the continuous and concurrent monitoring of a broad spectrum of behavioral responses including various measures of arousal, environmental interaction, and ingestive behaviors. The proposed research represents a systematic progression of studies designed to assess the role of EOS in the various behavioral components associated with different types of degrees of stress. The acute and chronic behavioral profiles of putative mu- (morphine, methadone), kappa- (ketocyclazocine, ethylcyclazocine), sigma- (+NANM, PCP), and delta- D-Ala^2-Met^5-enkephalinamide) opiate receptor agonists will be characterized in the RACs as will the relatively pure opiate antagonists naloxone, naltrexone, and diprenorphine. Under identical experimental conditions, the effects of restraint, noise, and exposure to a novel environment will be determined. Acute interactions and crosstolerance/sensitization between opioid and stress effects will be examined to determine the extent to which similar behaviors induced by these treatments are mediated by common underlying mechanisms. The detailed acute and chronic behavioral characterization of exogenously administered opioids and various stressors should enhance our understanding of the role of EOS in the regulation of responsiveness to stress. The potential clinical value of this research is indicated by the accumulating evidence that stress may be significantly implicated in the pathogenesis of major forms of psychopathology including depression and schizophrenia. In addition, individual differences in responsiveness to stress may be involved in determining predisposition to drug abuse.

RESEARCH PROJECT #2: **BEHAVIORAL PHARMACOLOGY OF ACUTE AND CHRONIC AMPHETAMINE**

PROJECT DATES: 06/29/76 -- 12/31/86

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

Thorough behavioral characterization of the acute and chronic amphetamine profiles in experimental animals is a necessary prerequisite for elucidating the psychological and neurobiological process implicated in amphetamine abuse liability and those affected by various patterns of usage in humans. In addition to the use of dosage regimens which simulate various abuse patterns, comparisons of psychomotor stimulants that produce effects in humans similar to amphetamine (e.g., cocaine) with those that do not (e.g., caffeine) may also provide useful behavioral and neurochemical information. Another approach involves the identification of behavioral dimensions that transcend species-specific responses, i.e., the perserverative quality of the response and the corresponding decreases in environmental interaction. Some evidence suggests that mesostriatal dopamine and serotonin systems may play a role in perseveration whereas the degree of environmental engagement may be regulated by a balance in the activities of the dorsal noradrenergic system and the mesolimbic serotonergic system. Studies with the selective monoamine lesions are designed to test these hypotheses. Converging evidence indicates that the appearance of specific components of the behavioral response to stimulants are intimately related to the experimental conditions, exhibit strict temporal patterns, and vary dramatically between animals. However, most biochemical studies have used pharmacologically, but not necessarily behaviorally relevant experimental conditions and the time points, and have ignored individual differences in response. More relevant biochemical data would be obtained in studies of individual animals whose behavioral profiles have been assessed. In addition, because of the limitations associated with post-mortem biochemical analyses, studies are also planned using push-pull perfusion techniques to measure synaptic transmitter levels in freely moving animals. This approach provides a continuous measure of neurotransmitter dynamics throughout the behavioral time course, and allows each animal to serve as its own control. Our ongoing and proposed studies represent a multidisciplinary approach aimed at characterizing the spectrum of stimulant effects produced by the range of dosage regimens associated with various patterns of stimulant abuse.

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Co-Principal Investigator

STEVEN J. HENRIKSEN, Ph.D.
GEORGE F. KOOB, Ph.D.

RESEARCH PROJECT: MORPHINE-LIKE BRAIN PEPTIDES: CELLULAR NEUROBIOLOGY

PROJECT DATES: 02/01/86 - 01/31/89

FINANCIAL SUPPORT: National Institute on Drug Abuse (NIDA)

DESCRIPTION OF PROJECT:

We propose to continue and extend our cellular neurophysiological studies by focusing on separate opioid-containing circuits within a major limbic network containing several loci of prodynorphin and proenkephalin-derived peptides. We shall do so by applying extra-cellular and intracellular recording techniques, both in vivo and in vitro, to selected portions of the entorhinal cortical-dentate-hippocampal-accumbens system, since work in our laboratory and others implicates these areas as important in self-stimulation and opiate-seeking behavior. The objectives of these studies will be to attempt to determine whether the opioid peptides within specific circuits of this system function as neurotransmitters, whether there are cellular correlates of opiate seeking behavior and whether the opioid peptides and relevant opiate receptors in this system are involved in such behavior. We shall pursue the first and third objectives in vivo by administering opiates, opioid peptides and specific opiate receptor antagonists by local iontophoresis and micropneumatic methods, and by the i.v. or i.p. systemic route. In vitro we will use superfusion of these substances and the same local application methods as in vivo. Endogenous opioids will be released in vivo and in vitro by electrode stimulation of opioid-containing pathways. Single-electrode voltage clamp methods will be used for analysis of the more covert voltage-dependent opioid effects. We shall record single units in nucleus accumbens in awake animals involved in a heroin self-administered protocol, to seek cellular correlates of opiate reward phenomena. For the final goal we will examine responsivity of neurons in this system to the opioid peptides after chronic treatment with morphine, in order to compare the naive state to that of the heroin-seeking state. We believe these studies will help unravel the role of the opioid peptides and their receptors in normal, opiate-seeking and opiate addictive behavior.

Co-principal Investigators

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S.L. BATKI, M.D.
S. BRUMMETT, M.S.W.

RESEARCH PROJECT #1: **FROM METHADONE MAINTENANCE TO ABSTINENCE**
PROJECT DATES: 04/01/81 -- 12/31/86
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This study investigates the impact of providing tapering and aftercare assistance to heroin addicts enrolled in methadone maintenance. Its specific aims are to:

1) Evaluate the effectiveness of a comprehensive outpatient program assisting methadone maintenance patients in tapering from methadone and remaining abstinent;

2) Identify the barriers to tapering from methadone maintenance among recovering patients motivated to detoxify; and

3) Study the process of tapering from methadone maintenance.

A pre- post-matched comparison group design will assess the program's impact on patients achieving detoxification from methadone, their drug and alcohol usage, treatment progress, treatment satisfaction, severity of problems associated with addiction, and assimilation into nondrug-using community. Fifty-five patients in three clinics receive written materials only. To achieve aim 2, patients who meet recruitment criteria for the tapering and aftercare program will be interviewed to assess barriers, motivations, and incentives to tapering, using a standard interview format that previously has not been administered to this group. Measures to accomplish specific aim 3 include amount of participation in essential and ancillary treatment activities, depression and withdrawal symptoms, and drug and alcohol use among patients in the experimental group.

This study is part of biopsychosocial efforts aimed at discovering ways to help former heroin addicts recover to a drug-free lifestyle.

Co-principal Investigators

G. BERNAL, Ph.D.
D.R. GIBSON, Ph.D.
L. WERMUTH, Ph.D.

RESEARCH PROJECT #2: **COMMUNITY NETWORK APPROACH TO DRUG ABUSE TREATMENT**

PROJECT DATES: 09/01/83 -- 08/31/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This project investigates the impact of training of family members to assist in the treatment of methadone maintenance patients. It occurs in a methadone program that requires applicants to have a nondrug using person who will "sponsor" their treatment. The specific aims are to test the impact of a 20-hour training program for sponsors and to examine family functioning in the early months of methadone maintenance. Seventy-five sponsors of methadone maintenance patients are assigned randomly to receive training or to a control group that receives no more than the standard treatment (monthly meetings of sponsors). Measures of impact focus on:

1) The sponsor (confidence in assisting the methadone patient in treatment, attitude toward methadone treatment, and knowledge about drugs and family dynamics);

2) The patient (drug use, counselor ratings, and treatment satisfaction); and

3) The relationship of sponsor and patient (intensity of contact, social network of nondrug-users, and willingness to attend joint counseling sessions).

A smaller group of sponsor-patient pairs provide additional measures of family functioning and severity of addiction at baseline, and shortly after the patient begins treatment.

The Community Network project is an outgrowth of research demonstrating the promise of family treatment with drug abusers. It reaches a wider population than others. This investigation is a part of a search for psychosocial treatments that modify drug abusers' support systems, making rehabilitation more possible.

Co-principal Investigators

S.L. BATKI, M.D.
D.R. GIBSON, Ph.D.

RESEARCH PROJECT #3: **SUBSTANCE ABUSE COMPONENT OF SUBSTANCE ABUSE AND MENTAL HEALTH IN AIDS CENTER**

PROJECT DATES: 09/30/86 -- 09/30/91

FINANCIAL SUPPORT: National Institute of Mental Health

DESCRIPTION OF PROJECT:

This is a component of the Substance Abuse and Mental Health in AIDS Research Center (Stephen Hulley, M.D. is Principal Investigator of the Center). The Substance Abuse component of the Center conducts clinical studies aimed at developing better methods to prevent and treat AIDS among intravenous drug abusers. Two new studies have been designed for this proposal:

1) **AIDS Prevention with Drug Abusers Completing Residential Treatment:**
We will investigate the impact of providing a psychoeducational intervention to intravenous drug abusers completing residential care, to reduce their chances of contracting AIDS or spreading the virus.

2) **Methadone Maintenance Impact on Sharing of Body Fluids by Seropositive Drug Abusers:**
We will test the effectiveness of a methadone maintenance treatment designed for seropositive opiate abusers, many of whom have AIDS or ARC. A pilot study will assess the program's effects on these patient's sharing of body fluids; a later study will compare an abstinence-oriented methadone maintenance, with a novel public health-oriented approach designed to attract and hold a broader spectrum of difficult-to-treat opiate abusers.

In addition, the component will provide pilot research support for studies emerging from collaboration during the time of the center grant as a way to stimulate research in substance abuse and AIDS and to take advantage of unusual research opportunities that are brought about by intergroup collaboration in the Research Center.

Co-principal Investigators

S.L. BATKI, M.D.
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E.S. MORALES, Ph.D.
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RESEARCH PROJECT #4: **AIDS PREVENTION WITH DRUG ABUSERS: A PSYCHOEDUCATIONAL APPROACH**

PROJECT DATES: 04/01/87 -- 03/31/89

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

This study investigates the impact of providing an educational intervention for intravenous opiate abusers to reduce their likelihood of contracting or spreading AIDS. The specific aims are to develop and test the impact of a 10-hour psychoeducational training program on:

- Increasing opiate abusers' knowledge about AIDS and the ways that HIV is spread;
- Changing attitudes that put them at risk for contracting or spreading the virus;
- Reducing the behaviors that put them at risk; and
- Reducing their substance abuse.

A long-term goal is to develop interventions that prevent opiate addicts from developing AIDS.

This preliminary assessment will develop and test the intervention in the Substance Abuse Services of San Francisco General Hospital. One hundred intravenous opiate abusers undergoing outpatient methadone detoxification and 60 intravenous opiate abusers in methadone maintenance will be randomly assigned to psychoeducational training or to a comparison group that receives written materials only. Measures of impact will focus on:

1) Information received;
2) Attitudes toward risk;
3) Behaviors that are high risk for contracting or spreading AIDS; and
4) Substance abuse.

Another set of measures will document treatment process, to help in subsequent revision of the intervention.

This study builds on research with other risk groups, attempting affective education and skill training rather than simply delivering information and warning about health risks. The study is part of an effort to prevent the spread of the AIDS epidemic among drug abusers.

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RESEARCH PROJECT: IDENTIFICATION OF OPIATE REWARD RECEPTORS
PROJECT DATES: 10/85 -- 06/88
FINANCIAL SUPPORT: National Institutes of Health, National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

We are attempting to identify via the self-administration and conditioned place preference paradigm, the specific opioid receptor type(s) which mediate the rewarding component of opiate abuse. This will involve use of specific antagonists and agonists for each of the identified opioid receptor types (mu, kappa, and delta). We will also endeavor to correlate information gained through this work with data existing in the literature concerning localization of receptor types in the brain. The animal model we will use is the Sprague-Dawley male rat. Currently proposed ligands include DAGO, DPro^{4}Morphiceptin, DADLE, DSLET, DTLET, D-Pen^{2}-D-Pen^{5}-Enkelphalin, D-Pen^{2}-L-Pen^{5}-enkephalin, dynorphin, Met-enk-Arg-Phe, U50488H, B-FNA, naloxonazine, TENA and diprenorphine. Self-administration experiments will be carried out in the ventricles as well as into discrete areas of the brain and will be accomplished both by Harvard pump systems and the electronic EMIT system.

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Co-principal Investigator

LINDSAY WOODARD, Ed.D

RESEARCH PROJECT #1: LOS ANGELES COUNTY HTLV-III SEROPREVALENCE STUDY

PROJECT DATES: 03/86 -- Present

FINANCIAL SUPPORT: L.A. County Department of Health Services

DESCRIPTION OF PROJECT:

Study in progress . . . 738 intravenous drug users were randomly sampled from all methadone clinics across the county. Blood samples were drawn for analysis and an extensive interview was conducted. It is anticipated that the study results will be available near the end of November, 1986.

Co-principal Investigator

BALKAR S. HUSSON, Ph.D.

RESEARCH PROJECT #2: **CURRENT TRENDS AND PATTERNS OF DRUG ABUSE IN LOS ANGELES COUNTY, 1982-1985**

PROJECT DATES: 1982 -- 1985

FINANCIAL SUPPORT: L.A. County Department of Health Services

DESCRIPTION OF PROJECT:

The report presents an analysis of the latest data available on trend indicators and patterns of drug abuse in the County. Data used include drug treatment admissions, drug-related emergency room admissions, drug-related deaths and seizures of drugs by police agencies.

Co-principal Investigator

DONALD McALLISTER

RESEARCH PROJECT #3: CLIENT OUTCOME FROM DRUG TREATMENT JANUARY 1984-DECEMBER 1985

PROJECT DATES: 1984 -- 04/1986

FINANCIAL SUPPORT: L.A. County Department of Health Services

DESCRIPTION OF PROJECT:

The report reviews drug treatment client outcomes in Los Angeles County. Outcomes include length of stay in treatment, discharge status, relapse rates, average time to relapse. Comparisons are also made by modality of treatment and major primary drugs.

Co-principal Investigator

RICHARD RUSSELL

RESEARCH PROJECT #4: **DRUG ABUSE TREATMENT CLIENT SATISFACTION SURVEY**

PROJECT DATES: Present -- 05/86

FINANCIAL SUPPORT: L.A. County Department of Health Services

DESCRIPTION OF PROJECT:

Seven hundred survey forms were distributed to clients from various treatment modalities for anonymous response. Of the 400 returned surveys, between 61 percent and 80 percent (depending on the agency) reported they found the services helpful, they would return if needed, they would want the same counselor, and they were very involved in planning their own treatment.

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RESEARCH PROJECT: PULMONARY EFFECTS OF HABITUAL, HEAVY MARIJUANA USE

PROJECT DATES: 07/01/82 -- 12/31/87

FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

The purpose of this cohort study is to determine whether heavy, habitual smokers (S) of marijuana (M) (>10 joints/wk, >5 yrs.) with or without tobacco (T) exhibit a greater longitudinal rate of decline in lung function and a greater frequency of development of lung function abnormality and symptoms of chronic bronchitis than a comparison group of lifelong never (or former infrequent) MS with or without T. The study groups will consist of 293 heavy, habitual MS and 149 non-MS examined in 1983-84 as part of a cross-sectional study of the pulmonary effects of heavy, habitual M use. Both the M-smoking and control subjects in the cross-section study will be invited to participate in a three-year follow up study, consisting of the annual administration over three years (1985-88) of an interval respiratory and drug use questionnaire and the same lung function tests that were performed at baseline. Methacholine inhalation challenges will also be performed to evaluate airways reactivity as a possible risk factor for development of marijuana-induced airways abnormality. To estimate the relative dose to the lung of M vs T smoke during customary smoking, we will also quantitate smoking topography and respiratory deposition of inhaled particulates in 20 MTS, 10 MS and 20 TS during smoking of M of low (~1%) and high (~3%) THC content and/or T of low and high nicotine/tar content. In addition, a subset of 30 M smokers (1/2 with and 1/2 without T), including 30 control nonsmokers of M (15 with and 15 without T) will be invited to undergo fiberoptic bronchoscopy with bronchial mucosal biopsy and bronchoalveolar lavage (BAL) a) to assess the presence and extent of histopathologic abnormalities in bronchial mucosal biopsies from smokers of M and/or T, and b) evaluate the effect of M (with and without T) on the lung's defenses.

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RESEARCH PROJECT #1: **RETENTION TIME OF ANABOLIC STEROIDS IN URINE**
PROJECT DATES: 1987
FINANCIAL SUPPORT: Community Health Projects, Inc.; Veract, Inc.; Los Angeles Dodgers: National Football League: Oak Tree Foundation

DESCRIPTION OF PROJECT:

Under control conditions volunteers are given anabolic steroids and the length of time that the steroid can be found in the urine is determined.

RESEARCH PROJECT #2: **STEP-WISE WITHDRAWAL TREATMENT FOR COCAINE AND NICOTINE DEPENDENCE**
PROJECT DATES: 1987
FINANCIAL SUPPORT: See Project #1.

DESCRIPTION OF PROJECT:

A number of neurotransmitter enhancers have been recently identified which appear to assist medical withdrawal from cocaine and nicotine dependence. The proper dosage and sequences of utilizing these agents are being systematically studied in order to develop clinical protocols for treatment of these drug dependencies.

RESEARCH PROJECT #3: **LAAM MAINTENANCE FOR PERSONS WHO FAIL METHADONE TREATMENT**
PROJECT DATES: 1987
FINANCIAL SUPPORT: See Project #1.

DESCRIPTION OF PROJECT:

Methadone maintenance patients who cannot maintain adequate plasma levels at a dose of 100 milligrams per day are being transferred to LAAM maintenance. Using plasma concentrations and other indicators of drug use, it is being determined whether LAAM can maintain some patients who fail methadone.

RESEARCH PROJECT #4: **URINE TESTING OF ADOLESCENTS BY PARENTS**
PROJECT DATES: 1987
FINANCIAL SUPPORT: See Project #1.

DESCRIPTION OF PROJECT:

Parents have begun to have their teenagers urine tested whenever they suspect that drug use has occurred. A pilot program has begun where parents can obtain this service on demand. Research data is being collected as to the advisability and results of this program. Data include percentage of those who test positive; types of drugs being used; quantities of drugs being used; and the percent of teenagers who appear drug dependent. Once identified as drug dependent, the teenagers must sometimes enter medical withdrawal treatment.

RESEARCH PROJECT #5: **IDENTIFICATION AND PREVENTION OF AIDS IN INTRAVENOUS DRUG USERS**
PROJECT DATES: 1987
FINANCIAL SUPPORT: See Project #1.

DESCRIPTION OF PROJECT:

Tested capability has been established to routinely test intravenous drug users who enter treatment. This includes IV cocaine users as well as heroin users. Once identified as having AIDS antibodies in plasma, the patient is placed in a special treatment unit for ongoing monitoring and treatment. In addition to determining prevalence of these antibodies and epidemiological characteristics, a major aspect of this study is to administer agents that may enhance the immune system and prevent patients from developing AIDS Related Complex and/or active AIDS.

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RESEARCH PROJECT: COCAINE CESSATION: TREATED AND UNTREATED
PROJECT DATES: 04/01/85 -- 03/31/87
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

The Cocaine Cessation Project is a research project to explore the social-psychological processes of cessation from cocaine abuse. Using a combination of quantitative/qualitative instruments the project has interviewed, as of August 7, 1986, 217 respondents (120 present users and 97 quitters). All subjects are located by means of the chain referral method. The study plans to test three sociological theories of deviance (differential association, control, and drift) but will also explore motivations for cessation, social conditions for use and cessation, various coping strategies employed, use of formal and informal resources, changes in social networks, changes in family relationships, legal statuses, and employment history.

Findings from the study about treated and untreated cessation can be useful in suggesting new and revised treatment strategies for cocaine abusers.

Co-principal Investigators

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ALLEN FIELDS, Ph.D.
JOHN A. NEWMEYER, Ph.D.
DONALD C. DES JARLAIS, Ph.D.
PAUL CASADANTE, M.D.

RESEARCH PROJECT: **HIV SEROPREVALENCE AND SEQUELLAE AMONG I.V. USERS IN TWO CITIES**

PROJECT DATES: 10/01/86 -- 09/30/89

FINANCIAL SUPPORT: U.S. Public Health Research Grant Award
National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

New York and San Francisco may be thought of as at equivalent stages with regard to the spread of HIV among gay males, but at different stages with regard to intravenous drug users (IVDUs). In New York City it is estimated there is a 50 percent seroprevalence of HIV infection among IVDUs, while the HIV seroprevalence of HIV among this group in San Francisco has been measured at a far lower level--9 percent. Thus, the two locations provide an opportunity to compare:

1) General knowledge about AIDS transmission and risks among IVDUs;
2) Prevalence and incidence of risk behaviors; and
3) Prospective monitoring of seroprevalence.

The two cities also provide a natural laboratory where assumptions about health education and AIDS prevention as well as the psychological impact of knowing HIV test results can be tested empirically. Four collaborative studies will be conducted in San Francisco and New York City. These research issues are:

1) Assessment of the status knowledge of AIDS risk factors and behaviors among intravenous drug users (IVDUs), and how this may change over time;

2) Prospective monitoring of the seroprevalence rates of HIV antibodies among IVDUs between two cities;

3) The psychological impact of knowledge of HIV antibody-positive status on IVDUs;

4) Factors that may mediate successful dissemination and utilization of AIDS risk-reduction messages for specific sub-populations of IVDUs.

Approximately 1,200 IVDUs per year will be recruited each year in San Francisco (400 from 21-day detoxification programs, and 800 from out of treatment populations). About 400 IVDUs per year will be recruited in New York from treatment programs.

Co-principal Investigator

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RESEARCH PROJECT: **NALTREXONE TREATMENT OF OPIATE DEPENDENCE**
PROJECT DATES: 01/01/83 -- 12/31/87
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

Open label controlled study of naltrexone's utility in the treatment of opiate dependence.

A one-year, controlled study of the effect of adding naltrexone to drug-free, recovery-oriented treatment of narcotic dependency is proposed. Sixty patients hospitalized for treatment of narcotic dependency at Merritt Peralta Chemical Dependency Recovery Hospital (a private, not-for-profit hospital in Oakland, CA), who give informed consent to participate in the study, will be randomly assigned to either a control group (30 subjects who, after discharge from the hospital, receive all program aftercare services plus twice-weekly urine testing) or the naltrexone group (30 subjects who, after discharge from the hospital, will receive all program aftercare services plus twice-weekly, nurse-administered doses of naltrexone). The two groups will receive the same amount of staff contact and will receive identical aftercare services during the one-year study. Subjects will be comprehensively assessed while inpatient and 3, 6, 9, and 12 months after discharge. Outcome measures are: results of urine screens (for opiates and other drugs of abuse), participation in aftercare group, retention time in treatment group, and psychosocial measures. Multivariate, between-group analysis will be used to determine the effect of adding naltrexone to recovery-oriented treatment. Discriminant analysis will be used to identify predictor variables which forecast successful or unsuccessful naltrexone treatment group outcome.

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OTTO VON LIERER, Ph.D.

RESEARCH PROJECT: **PILOT PERFORMANCE AND TETRAHYDROCANNABINOL**
PROJECT DATES: 09/85 -- 08/88
FINANCIAL SUPPORT: National Institute on Drug Abuse

DESCRIPTION OF PROJECT:

We intend to study the effects of delta-9-tetrahydrocannabinol (THC, marijuana) on aircraft pilot performance. To date only one study has examined the effects of THC intoxication on piloting. This study used ten subjects and subjective observer-based check-sheet ratings as the dependent measures. No measurements were made of blood or urine THC metabolites in relation to performance nor were performance decrements related to change in basic psychological components. Given the widespread recreational use of THC in both private and military sectors, obtaining more detailed data about its effects on pilot performance seems warranted.

For the next year we propose to continue examining the effects of THC on pilot performance using our newly developed computerized flight simulator laboratory, which is specifically designed to study pilot performance. The independent and dependent variables studied in these experiments were selected on the basis of existing findings and their ecology validity, i.e., their relevance to actual piloting performance. The dependent measures are collected on a set of cognitive, behavioral, and flight performance variables. All four experiments share a subset of three independent variables:

1) THC dose level;
2) Task difficulty; and
3) Delay period between THC dose and test (up to 48 hours later to test for "hang over" effects.

Experiment I we are currently conducting addresses the effects of these three variables plus the pilot's level of recreational use of THC on performance.

Experiment II asks what effects these three variables plus pilot fatigue have on performance.

Experiment III looks at the effects of these three variables plus flying experience on pilot performance.

Experiment IV asks what effects these three variables plus age of pilot have on performance.

JEROME A. YESAVAGE, M.D.--PILOT PERFORMANCE AND TETRAHYDROCANNABINOL, (Continued)

In these experiments, we are particularly interested in the interactions of the four variables studies. We expect to complete Experiments I and II in the coming year.

Presently, little is known about the effects of THC on piloting, even though research, especially on driving performance, sugests that the drug may have its greatest and longest lasting effects on behaviorally and cognitively complex tasks. Just as automobile driving performance research revealed effects of THC not found in studies of simpler tasks, we expect studies of the even more complex task of piloting to reveal effects not found in driving.

THE RESEARCH ADVISORY PANEL

Experimental programs which use marijuana, hallucinogenic drugs and other controlled substances, as well as research concerning the treatment of narcotic addiction have operated in California since 1969 under the aegis of the Research Advisory Panel. The Panel was created by the Legislature to encourage research with marijuana and hallucinogenic drugs. Protocols for individual research projects concerning controlled substances are reviewed and approved or disapproved by the Panel. As part of the Panel's supervisory responsibility, ongoing projects are monitored and approval may be withdrawn if activities deviate significantly from the approved protocol.

The Panel also encourages and supervises research into treatment of controlled substance abuse, e.g., heroin addiction. Several new therapeutic medications have been evaluated in California, including levo-alpha-acetylmethadol (LAAM), propoxyphene napsalate (Darvon-N), clonidine hydrochloride (Catapres), guanabenz acetate (Wytensin), and naltrexone.

In 1979, the Legislature directed the Panel to sponsor a statewide study of the therapeutic value of cannabis and its derivatives in patients who experience nausea and vomiting due to cancer chemotherapy and in patients with glaucoma. Thus the Panel also functions as the sponsor (vis-a-vis a regulatory authority) of cannabis research.

The Legislature created the Panel as an independent review body composed of uniquely qualified individuals. The statute stipulates qualifications for certain members and requires that membership include oncologists, opthalmologists, psychiatrists, registered nurses, pharmacologists, physicians having either experience in drug abuse treatment or controlled substance research, and/or persons with doctorates in the health sciences field. Because of its diverse composition, the Panel functions as a peer review body in the manner in which it conducts business.

For further information contact the Panel directly:

Research Advisory Panel
6000 State Building
San Francisco, CA 94102

David Schieser, Ph.D.
Executive Secretary

The above description was taken from the Fourteenth Annual Report of the Research Advisory Panel, prepared for the Governor and the Legislature.

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

The basic research projects on AIDS are not included in this Directory. However, since the use of hyperdermic needles has been implicated in AIDS infections, we have included AIDS Research that involves intravenous drug use.

Readers interested in AIDS research should contact AIDS Clinical Research Centers, at this time at University of California--San Francisco or Los Angeles--or other researchers at the University of Southern California, University of California--Berkeley, Davis, San Diego, Irvine, or Santa Barbara. The Communicable Disease Control Section of the San Francisco Department of Public Health is familiar with the epidemic and work being done concerning AIDS. Knowledgable researchers may be found at the Haight-Ashbury Free Medical Clinic.

An Office of AIDS, under the California Department of Health's Preventative Medical Unit is located at 1812 14th Street, Sacramento, CA 95814, phone (916) 445-0553. Another resource is the Clinical Medicine Branch, National Institute of Drug Abuse, Room 10A-08, Rockville, MD 20857, Phone (301) 443-1801.

AUTHOR INDEX

ALKANA, R.L., 1, 2
AMES, G.M., 3,4,5
ANGLIN, M.D., 70, 71, 72, 73
ASTON-JONES, G., 15, 52

BARCHAS, J.D., 6
BATKI, S.L. 113, 115, 116
BAUMRIND, D., 74
BERNAL, G., 76, 114
BIERNACKI, P., 104
BIKLE, D., 7
BITONTI, C., 65
BLOOM, F.E., 8, 9, 15, 95
BRANNON, B.R., 86
BRILL, N., 40
BROWN, J.K., 78
BROWN, S.A., 10, 11
BRUMMETT, S., 113

CAETANO, R., 12
CASADANTE, P., 126
CASTAGNOLI, N., 79
CERVANTES, R., 16, 17
CHO, A.K., 80
COLEMAN, V., 36
CORBETT, K., 4

DES JARLAIS, D.C., 126
DEVINE, M.L., 81
DIAMOND, I., 19, 20

EHLERS, C., 9, 13, 15, 39, 51
ELLICKSON, P.L., 83
EL SHAMI, A.S., 82
ELMASIAN, A., 39
EPSTEIN, L.G., 14
ESTEP, R., 66
ETTENBERG, A., 29

FAULL, K.F., 6
FELDMAN, H., 104
FIELDS, A., 126
FIELDS, H., 84
FISCHER, J.R., 101
FLAY, B.R., 85, 86
FLORES-ORTIZ, Y., 76
FOOTE, S., 15, 39
FRAWLEY, P.J., 87

GARCIA, R.S., 102
GEBERS, M., 56
GEYER, M.A., 88
GIBSON, D.R., 114, 115, 116
GILBERT, M.J., 16, 17, 18, 20
GOLDSTEIN, A., 89
GORDON, A.S., 19, 20
GORELICK, D.A., 21
GRAHAM, J.W., 24
GREENBERG, D.A., 22
GROUL, D., 52

HALSTEAD, C.S., 23
HANSEN, W.B., 24, 85, 86
HELANDER, C.J., 25
HENRICKSEN, S., 9, 52, 112
HERD, D., 12
HILTON, M.E., 26
HOLDER, H.D., 27
HSER, Y., 71
HUSSON, B.S., 119

IRWIN, C.E., 67

JANKE, M., 44
JOHNSON, C.A., 85, 86
JONES, R.T., 90, 91, 92, 93, 94

KAUSHALL, P., 39
KING, L., 68
KIPROV, D.D., 104
KLATSKY, A.L., 28
KLEE, L., 5
KLITZNER, M.D., 14
KOOB, G., 13, 29, 95, 96, 112

LEE, N.M., 97
LIDDLE, H.A., 98
LOH, H.H. 99
LOWE, L., 30

MALONE, M.H., 100
MATOS, F.F. 100
McALLISTER, D., 120
McCLOSKEY, C.M., 101
McGIVERN, R.F., 31
MEDICINE, B., 32
MILLSTEIN, S.G., 67
MILNER, R., 33
MOORE, J.W., 102
MOORE, R.A., 82
MOOS, R.H., 34, 35

MORA, J., 4
MORALES, E.S., 116
MORGAN, D.G., 103
MORRISON, J., 15, 33
MOSHER, J.F., 36
MOSKOWITZ, J., 37
MURPHY, S., 107

NASATIR, D., 38
NEWMEYER, J.A., 104, 126
NEVILLE, H., 15, 39
NOVACK, J.A., 66

O'CONNOR, M.J., 40

PADILLA, A.M., 18
PAIGEN, K., 41
PARKER, D.A., 42
PARKER, K., 98
PFEFFERBAUM, A., 43
PLOTSKY, P., 45, 58
POLICH, J., 8, 39
PRYOR, G.T., 106

RAPOPORT, H., 105
RATZ, M., 44
REBERT, C.S., 106
RIVIER, C., 45, 58
RIVIER, J., 58
RODES, J., 55
ROIZEN, R., 46
ROOM, R., 47
ROSENBAUM, M., 107
ROTH, R., 36
RUSSELL, R., 121

SABA, G., 98
SADAVA, D., 108
SADEE, W.,109
SALTZ, R., 5, 48
SCHEIER, L.M., 73
SCHWARTZ, J., 29
SCHUCKIT, M.A., 49, 50, 51
SEGAL, D.S., 110, 111
SIGGINS, G., 52, 112
SIGMAN, M., 40
SINGER, T.P., 79
SMITH, D.E., 127
SMITH, S.K., 82
SORENSEN, J.L., 76, 113, 114, 115, 116
SPECKART, G.R., 72

STALL, R., 57, 69
STAUNTON, D., 52
STEPHENS, C., 53, 54, 55
STEVENS, K.E., 117
STEWART, K., 14
STRANTZ, I.H., 118,119,120,121

TASHIMA, H., 56
TASHKIN, D.P. 122
TEMPLE, M.T., 57
TENNANT, F., 123, 124
TREVOR, A.J., 79

ULENE, A., 86

VALE, A., 45, 58
VAN DER KOOY, D., 29
VON LEIRER, O., 62, 128
VOURAKIS, C., 59

WADE, C.H., 73
WAGENAAR, A., 60
WALDORF, D., 125
WATTERS, J.K., 104, 126
WAY, N., 98
WEISNER, C., 61
WENGER, J., 29
WERMUTH, L., 114, 116
WESSON, D.R., 127
WOODWARD, L., 118

YESAVAGE, J.A., 62, 128
YOSHIDA, A. 64

S U B J E C T I N D E X

ALCOHOL

AGE GROUPS:	5, 10, 26, 30, 43, 57
AIDS:	69
ANIMAL STUDIES:	1, 2, 6, 13, 15, 23, 29, 31, 33, 39, 41, 52, 58
CHEMISTRY/BIOCHEMISTRY:	1, 2, 6, 9, 13, 15, 19, 20, 22, 23, 29, 33. 39, 43, 45, 50, 52, 58, 64, 93
DRIVING/FLYING UNDER THE INFLUENCE:	14, 25, 27, 36, 44, 56, 60, 62
ELDERLY:	35, 57
EMERGENCY ROOM:	53, 54, 55
ETHNIC GROUPS:	4, 5, 12, 16, 17, 18, 30, 32, 68
FAMILY:	3, 4, 8, 27, 65, 68
FETAL ALCOHOL SYNDROME	31, 33, 40, 55
GENETICS:	8, 39, 41, 50, 51, 68
HEALTH/DISEASE:	7, 11, 23, 28, 42
INFANTS:	33, 39, 40, 55
LEGAL:	36, 61
PREVENTION/INTERVENTION:	3, 21, 24, 26, 27, 36, 37, 48, 65, 83
PROGRAM EVALUATION:	24, 25, 27, 34, 37, 48, 56, 65
SEX:	5, 26, 30, 31, 32, 50, 51, 58
SOCIAL/BEHAVIORAL:	4, 5, 11, 12, 15, 16, 17, 21, 26, 29, 35, 46, 47, 61, 62, 66, 67
TREATMENT:	10, 17, 21, 34, 46, 49, 59, 61
WOMEN:	5, 16, 40, 55, 59, 65
YOUTH:	10, 24, 27, 37, 38, 50, 67, 83

S U B J E C T I N D E X

DRUGS

AGE:	103
AIDS:	69, 104, 115, 116, 118, 124, 126, 131
ANIMAL STUDIES:	88, 93, 95, 103, 106, 108, 109, 111, 112
CANNABIS:	81, 90, 91, 101, 106, 122, 128
CHEMISTRY/BIOCHEMISTRY:	76, 79, 80, 84, 88, 89, 91, 92, 93, 94, 95, 96, 97, 99, 100, 103, 105, 109, 110, 112, 116, 117, 123
COCAINE:	82, 87, 92, 96, 123, 125
ETHNIC GROUPS:	68, 71, 76
FAMILY:	66, 68, 74, 76, 86, 98, 102
HALUCINOGENS:	79, 80, 88
HEALTH/DISEASE:	79, 103, 122
LEGAL/CRIMINAL	70, 71, 72
METHADONE:	107, 108, 113, 114, 115, 118, 123
OPIOIDS/NARCOTICS:	70, 71, 76, 82, 84, 89, 95, 97, 99, 100, 101, 105, 109, 110, 112, 113, 114, 115, 116, 117, 118, 127
PCP	79, 80
POLYDRUG-MULTIDRUG:	73, 78, 83, 93, 94
PREVENTION/INTERVENTION:	37, 65, 72, 74, 83, 85, 86, 115, 116, 126
PROGRAM EVALUATION:	85, 98, 113, 114
SEX:	71, 102
SOCIAL/BEHAVIORAL:	66, 67, 70, 73, 94, 102, 119
STIMULANTS:	111
DRUG TESTS:	82, 124

TREATMENT:	70, 76, 81, 87, 98, 107, 113, 114, 120, 121, 123, 125, 127,
TOBACCO:	83, 85, 86, 123
WOMEN:	65, 71
YOUTH:	37, 67, 74, 83, 85, 98, 124
DRIVING/FLYING UNDER THE INFLUENCE:	128